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Original Communications

HONESTY AND COURAGE CAN ERADICATE TUBERCULOSIS

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FIVE million or more persons die every year from tuberculosis. Five hundred thousand die in India alone.

In the Philippines over 35,000 deaths occur annually, one every fifteen minutes. Over a million more have tuberculosis, and the population is only eighteen million. In the slum areas, children below 2 years old are 80 per cent positive, and between 3 to 4 years of age, 100 per cent.

In Poland one out of every ten persons has active tuberculosis. Similar or worse conditions exist in many parts of the world. In many areas mortality rates from 500 to 800 per hundred thousand are reported.

In the September issue of the *National Tuberculosis Association Bulletin*, Perkins stated there were over 500,000 persons in the United States with active tuberculosis, more than one-half of whom are not known; the exact number could *be larger. Certainly the tuberculosis decline is lagging far behind other communicable* diseases, yet we are told tuberculosis is under control.

In the United States, case-finding programs, hospitalization, isolation, and treatment are among the best in the world, but about 50,000 die here every year. Moreover, our country contains only 5 per cent of the world's population and cannot be isolated. The world is getting smaller. It can now be circled in about three days. The tubercle bacillus knows no boundary lines. Thousands of our citizens travel all over the world and people from other countries are coming into ours. In many places, certificates of health against smallpox, typhoid. etc., are compulsory, but for tuberculosis there are no barriers.

In the past year I have *traveled about 75,000 miles by air visiting Asia and* Europe, as well as Hawaii, the Philippines, South and Central America, and have had definitely impressed upon me that nothing worthy of being called *tuberculosis control exists. My pilgrimage, plus my intimate association with this* disease for many years, has convinced me that if we are ever successfully to combat it, we must approach the problem with a much broader vision than we have in the past. Some of my observations I should like to leave with you today.

Presidential address, Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15, 16, 17, and 18, 1950.

In poverty stricken India people live in cubbyholes, often with cows, goats, manure, etc., and under such crowded conditions that they sleep in rows. Much malnutrition exists, and hygienic conditions are nonexistent. There are only 127 beds for tuberculosis in the large city of Delhi, and 7,500 in all of India. With hopelessly inadequate numbers of hospital beds, surgeons, and medical men, proper treatment is absolutely impossible.

In Japan, the badly overcrowded housing, the hygienic conditions, poverty, and malnutrition are almost as bad. Some good surgery is done, and there are some good hospitals, but most of the treatment of tuberculosis consists of ambulatory pneumothorax at medical centers. They have a center for every 100,000 persons. I found that only 60 per cent of the patients treated had positive sputum when pneumothorax was started, and only 50 per cent were converted by treatment. All of these are living at home infecting others.

In China, with the Communists overrunning most of the country, no official figures were available, but I was told by Chinese doctors that in many parts 30 to 50 per cent of the population have tuberculosis. There are only 300 beds in all Hong Kong. The Minister of Health told me that most patients got well while at work and without treatment in a period of about six months. I leave this with you without comment.

In the Philippines I was told by Dr. Arguellis, to whom I am indebted for considerable statistical material, that the mortality rate is about 170 per 100,000 in rural districts, and about 270 per 100,000 in Manila proper. There are some good hospitals there, but it is economically impossible to adequately care for tuberculosis.

In Siam there are only a few fifty-bed hospitals. The same story of poverty, bad sanitation, etc., exists. No attempt is made to control tuberculosis. Ambulatory pneumothorax again is the principal treatment. The mortality rate, I was told, was 275 per 100,000, but it is no doubt higher.

In Egypt proper facilities simply do not exist. Estimates on mortality rates varied from 200 to 300 or over per hundred thousand. I left Egypt with only the knowledge that little or nothing is done for the tuberculous except ambulatory intra- or extrapleural pneumothorax, and as in other countries abroad, some streptomycin for the rich. I am sure nobody knows what the real situation is, and it was my feeling that they do not care.

When Hitler came to power in Germany he threw out many of the best doctors who were not Nazis. When we took over, we threw out all the Nazis. There are many doctors there who have had only nine months of college education. Shortly after our occupation, efforts were made toward the management of tuberculosis in British, American, and French Zones, but when Clay and Hawley took over, I am told, the medical personnel representing the United States was cut from 174 to 7. In October, 1949, we had no doctor in either Berlin or Bremen. In fact, there was no longer a Department of Health. This had been put under welfare and education, and instead of doctors, there was an influx of ministers, teachers, movie actors, etc. I am informed that McCloy has made it possible for Col. Lundeberg and Col. DeForrest, Dr. Benning, and others who represent us in Germany, to again encourage active measures.

Statistics there are practically worthless. Tuberculous persons get increased rations and German doctors are willing to cooperate and diagnose tuberculosis where it does not exist. Their decrease in mortality rate is, in my opinion, partly *due to few post-mortems, and change in the classification of deaths.* One such classification is senility. How many of these died of tuberculosis is anybody's guess. A prominent German doctor stated to me that there were 25,000 active cases living at home in Berlin alone, with the consent of the authorities, because tuberculosis was not considered communicable in the adult stage. From 70 to 90 per cent of the cattle there are infected. Milk is sold on the streets out of pails. It is also skimmed and fed to calves, hogs, etc. Therefore, a good percentage of these now have the disease. With fraternization going on between our troops and the German girls, tuberculosis is quite a problem for us in Germany. Dr. Esmond Long stated that every American soldier contracting tuberculosis there costs the United States government $30,000. In Germany, as in most countries abroad, streptomycin and para-aminosalicylic acid (PAS) have been used mostly for meningeal and miliary tuberculosis. TB(1) in Germany has been used in less than 10,000 persons, and the results are not convincing. It is *used mostly for bronchial, intestinal, and glandular tuberculosis.*

In Copenhagen, excellent conditions exist. One-quarter of the whole population is x-ray or tuberculin tested every year. Everybody is examined, therefore, every four years. Their mortality rate of 34 per hundred thousand is among the lowest in the world, but tuberculosis is still the great killer there. In Rumania, Czechoslovakia, and Austria they report the use of an antigen called tuberculomucin, but its real value has not been established.

In Italy, France, England, and Ireland, the conditions are better than they are in Central Europe, but still very bad. Ambulatory pneumothorax is the national pastime. In Italy, Dr. Pasluci, Dr. Monaldi, and others are excellent surgeons, but a proper program of tuberculosis control does not exist.

In Switzerland, where the conditions should be ideal, the mortality rate is still about 67 per hundred thousand. They have good hospitals and doctors, but thousands there are still dying from this disease.

In South and Central America as in all of Europe and Asia the treatment of tuberculosis is not much more than a gesture. Ambulatory pneumothorax is the only treatment that can be used on a large scale. Time and space prevent a detailed report on all the countries I have visited, but, in a general way, their problems are the same and tuberculosis eradication is still a dream of the long distant future.

President Roosevelt was certainly ill advised when, a number of years ago, he said, "Now that we have tuberculosis under control, we must begin on cancer." One wonders whether, when we discover the cause of cancer, we shall be as apathetic and lethargic in applying our knowledge to treat this disease as we are with tuberculosis.

There is no need to mention the great strides made in the surgical treatment of this disease. It is rather its improper use upon which I should like briefly to dwell. Surgery plays only a small part in the over-all picture of tuberculosis eradication, but it, together with antibiotics and other measures now employed for salvage, will be for many years to come an essential and integral part of our program. The millions of persons now living, and the millions more to follow who may contract this disease, however, should be our greatest concern. For these we are doing very little. We, as surgeons, are really working on the wrong end of the line, trying to overcome the ravages of a communicable disease that should not exist.

We have all been lulled into a sense of false security by the repeated statements that tuberculosis is on the decline or is "under control." We go on our way embellishing techniques or substituting some new bizarre, and often ridiculous, measures which accomplish less than the ones they were intended to supplant. In my recent world tour, I saw and heard of many such procedures. These are frequently used also in this country.

Pneumothorax is rapidly being discarded as a procedure of choice. Its many complications of fluid, empyema, frequent inability of lung re-expansion following its use, together with the inability to determine the condition of the lesion in the collapsed lung, impossibility of knowing when to discontinue it, etc., have convinced most observers that it should be virtually abandoned. It is still used routinely, however, in some places, often being carried on for years with the patient at home, with positive sputum under ineffective collapse. The same is true of pneumoperitoneum.

I have discussed intrapleural pneumothorax at length because the same complications that follow its use are also encountered in the surgical procedure, extrapleural pneumothorax. When the extrapleural space is maintained by air, these complications are about the same as just described, but many surgeons are not satisfied with this debacle and fill the space with all sorts of foreign bodies. Those most frequently used are Gomenal, paraffin, and Lucite balls. Gomenal sometimes develops into a pus poultice. Many years ago I had two patients drown following its rupturing into a bronchus. Paraffin may also rupture into the bronchus or become infected, and frequently does. Lucite balls, from pressure and necrosis, sometimes rupture into the mediastinum, the other hemithorax, the neck, or any place available. At Duke University years were spent digging out these balls, but today many surgeons are still using them routinely. The use of these procedures is haphazard, unscientific, inexact, and inexcusable. We have all seen even small cavities change in position, but not in size, under a 90 per cent collapse with pneumothorax or thoracoplasty. How, therefore, can anybody without Divine guidance know how much paraffin or how many Lucite balls will be necessary to cause cavity closure. Furthermore, once they are put into the space, they obscure the x-ray examination and one cannot tell whether cavities are closed or not. If they are still open, further attempts to close them might be extremely hazardous. Nature, however, apparently rebels at the presence of foreign bodies, and seeks to eject them in one way or another. There are some few isolated cases, with extensive collapse in the contralateral lung and low respiratory reserve, with a small cavity high up in the apex of the other lung, where a small pack might be excusable, but their routine use should be abolished.

Our best results are usually found following thoracoplasty. Tuberculosis is a systemic disease, and therefore when it seems probable that thoracoplasty can accomplish the desired results, it is preferable to resection. There are numerous lesions not amenable to it, however, such as tuberculous bronchiectasis, stenotic bronchi with diseased lung beyond, coin and round lesions, and parenchymal lesions that cannot be differentiated from carcinoma. In numerous other conditions in which resection might be preferable there is a great difference of opinion. I hope this may be standardized as much as possible.

The greatest number of lung resections are done for the group of patients whose cavities remain open after thoracoplasty. I should like to discuss this group in more detail. Cavities still remaining open after this procedure are often due to bad thoracoplasties, and ridiculous embellishments of it. The use of small or multiple incisions, working in the dark to dig ribs out of a tunnel, failure to remove transverse processes, the use of all sorts of temporary packs between stages to overcome failure to remove sufficient lengths of ribs overlying the cavity are the most frequent causes of failure. If a good clean thoracoplasty, done under good vision, is performed, with the removal of all transverse processes including the first, and the complete removal of at least the first three ribs to the cartilages including the first cartilage from behind, and the remaining ribs far in front, there will be fewer anterior stages necessary, and a marked reduction in the number of residual cavities that require resection. After a bad thoracoplasty with cavities still remaining, we are confronted with the difficult decision of either doing several stages of revision, plus probable removal of more ribs, or of resecting. The patient has, by this time, been subjected to a lot of fruitless and unnecessary mutilation after which resection and death sometimes occur needlessly because proper surgery had not been done in the first place. The patient's respiratory reserve will, of course, require some modification of this ideal procedure.

Some surgeons use an anterior stage as the first procedure. Most cavities are situated posteriorly. If a thoracoplasty is properly done from behind, this stage is often not required. Some surgeons use it routinely after two or three posterior stages, regardless of the location of the cavity, or that an insufficient number of ribs have obviously been removed, with the cavity plainly visible posteriorly, directly under the unremoved ribs that are holding it open. By this time the rebridged bone, in the upper decostalized area, is so firm that an anterior stage is practically useless.

The Monaldi operation and cavernostomy have been practically discarded throughout the world, except for symptomatic relief or preparatory to thoracoplasty. In my travels I found only Monaldi himself advocating his procedure in preference to thoracoplasty, resection, etc. In Vienna, Denk is very partial to cavernostomy, but he was the only one I found who favored it. However, there are still some few surgeons who are using these procedures routinely in America.

I find reports of permanent paralysis, following crushing of the phrenic nerve, varying from 5 to over 20 per cent, depending upon the technique used. In some clinics, the nerve and sheath were macerated by 7 or 8 crushings; others tied silk tightly around the sheath to make identification easier on a second crushing. Many other insults to the nerve and sheath have been perpetrated. Actually there is necessity for only one crushing of the nerve with a fine forcep and severing of small accessories. If the accessory nerve is a large one, it only should be crushed in my opinion. If small incisions and careful dissection are used I believe permanent paralysis will occur in not much more than 1 per cent. With recrushings and those done in conjunction with pneumoperitoneum, the percentage will be somewhat higher.

Streptomycin, PAS, etc., have in this country completely revolutionized the surgical treatment of this disease, but so much has been written on this subject that I shall not discuss it here. Waksman's recent book contains a chapter on the subject which I wrote.

It has been determined, however, that patients with tuberculous cavities, become resistant to streptomycin much earlier than those without them. It is imperative, therefore, that with cavitation some form of collapse be given simultaneously with streptomycin. In unilateral lesions, phrenic operations and thoracoplasties are the procedures of choice, but in bilateral lesions, pneumoperitoneum may be utilized until one side becomes stable, and it can be determined what permanent procedure, if such is necessary, may be performed.

In spite of surgery and our present antibiotics, however, we are not getting tuberculosis under control, for no matter how many we salvage the host of new victims are forever surging onward with a horrible toll. The hoped for benefits from case finding and hospitalization are rarely achieved for, in most or all places, such scarcity of hospital beds exist that it sometimes appears futile to find active cases when little can be done about them when they are discovered. This condition will always exist in most parts of the world. After hospitalization has been accomplished many patients leave against medical advice and go back to their homes, again spreading tuberculosis to all with whom they are in contact. The stupid requirements for nurses' training also adds to our difficulties. Thousands of patients with positive sputum roam the streets awaiting admission to sanatoria, which is denied them because of deficient nursing personnel. Case-finding programs are usually haphazard, sporadic affairs carried on in the most densely populated areas, and in schools, with a great bulk of the population not reached.

It is argued that in the United States with its relatively low mortality rate further measures are unnecessary. However, about 50,000 die of tuberculosis here every year and 500,000 or more have active disease. The incidence of tuberculosis seems to me to be of more significance than death rates; and we have no proof that the incidence is on the decline. Death rates fluctuate with economic conditions, wars, facilities for isolation and treatment, inherent and acquired resistance, etc., and cannot be an accurate guide to incidence. The examination of millions of draftees in the last war should have caused a tremendous decline in both mortality and incidence. Lack of hospital beds for active cases, however, counteracted much of the expected results. Many individuals also with known disease refused to be hospitalized during this period, because of high wages paid for labor, and remained at work, living with their families spreading disease until it was too late for treatment. This practically nullified the results of this mass survey. In the last few years the use of streptomycin, PAS, and surgery have caused a drop in death rates. Many whose deaths have been retarded by these measures, however, will die later and cause an upswing in mortality rates. In the war-torn countries of Europe, the recent reduction in death rates is only apparent, not real. Many individuals who under normal conditions would have lived through the peak of the high death rates of 1945 and 1946 died prematurely from lack of heat, food, light, etc., causing an upswing in mortality rates. Following their deaths there would obviously be a drop in death rates, for most of the very ill individuals were gone and there were left those with early lesions, and disease in those persons who had sufficient resistance to overcome all these hardships. The mortality rates may soon turn upward again unless some other methods are employed to combat the disease.

Let us suppose, however, that our present methods are sufficient and we can actually rid our country of active tuberculosis. Negative tuberculin reactions and lowered resistance increase as active tuberculosis decreases so we would then develop a race of individuals like the Eskimos, Indians and Negroes who because of lack of contact with tuberculosis have little resistance to it. It would not be long before this new race would die from tuberculosis like rats caught in a trap created by us. Many observations seem to confirm the probability of this occurrence. One of the most interesting of these occurred on the Island of Bornholm, where the incidence of tuberculin negative individuals was the highest in Denmark. When these persons went to other countries, or areas where tuberculosis was more prevalent, and returned, an alarming rate of active tuberculosis was found among them. This continued until tuberculin negatives were converted to positive before leaving the island. We cannot completely stop the constant flow of people to and from other countries. The more we decrease the incidence of tuberculosis in one country, or parts of it, therefore, the greater is the need for protection to tuberculin negative individuals. Unless we use vaccination as in smallpox, diphtheria, etc., there is, in my opinion, no hope of ever obtaining this protection, without which the eradication of tuberculosis is impossible. We have such a vaccine available, but through ignorance of its efficiency, misunderstandings regarding its harmlessness, prejudice, jealousies, lethargy, and apathy, its use has been neglected. That vaccine is B.C.G.

There can be no question at the present time as to the efficiency and harmlessness of B.C.G., but its development has been a slow process. When Koch discovered the tubercle bacillus in 1882, the conquest of tuberculosis was thought to be within our grasp. He found that a guinea pig, already tuberculous, was resistant to a second tuberculous infection. The original infection ran its usual course, but a second inoculation produced only a local reaction, and healed rapidly. This is Koch's phenomenon. Healed lupus also produces protection against tuberculosis. These discoveries made it quite clear that increased resistance to and prevention of tuberculosis could be accomplished if a safe method were discovered to produce it. Tuberculin was tried at first. Many workers also tried dead tubercle bacilli, but all were disappointed with the results. Experimental work, however, is still going on with dead bacilli, and also with the vole bacillus of wells. The use of live tubercle bacilli was then started. All sorts of experiments were made and conflicting reports appeared in literature. It was not until Calmette and Guérin in 1908, using the Nocard's bovine strain of the tubercle bacillus from the udder of a cow, that real progress was begun. At the start of these experiments toward the attenuation of the live bacillus, it was so virulent that 3 mg. injected into calves produced death in 5 to 6 weeks. However, after 30 passages on glycerine bile potato medium every 25 days, it became innocuous for calves. Eleven years after the start it became innocuous for guinea pigs which have practically no resistance to tuberculosis. In 1924, Calmette declared it a "Virus Fixe" which would remain avirulent. This was accomplished after 230 subcultures of the strain had been made. To insure this avirulence constant assaying of cultures is necessary. In 1927, Petroff published his work and claimed he had grown a virulent variant called "S" from Calmette's B.C.G. culture as well as the "R" which was avirulent. The political and personal squabbles and jealousies that followed between men and nations were disgusting and are too numerous to mention. Some supported Calmette and others Petroff; others had views of their own. Much confusion existed, but Calmette, Guérin, and their followers remained firm in their belief and vaccination of human beings continued. In 1930, the Lubeck disaster occurred which shocked the world and did a great deal to destroy confidence in B.C.G. So much confusion existed then and still persists that a detailed report of the incident I feel is necessary.

Early in 1930, 249 infants were vaccinated in the town of Lubeck, Germany. The vaccine used was a culture of B.C.G. from the Pasteur Institute. Later 73 infants died. Criminal proceedings were started and all vaccinations were stopped. Investigators found first that the strain from which the vaccine came was avirulent when it left the Pasteur Institute, and to this day it has remained so. A vaccine made from the same culture had been given to infants, in another city, at the same time and there were no untoward results. Cultures were made from autopsy material and the organisms grown were of the human type. B.C.G. is from bovine tubercle bacillus. In the laboratory at Lubeck there was a human culture from Kiel. When the Kiel culture was grown on boullion it gave a green color which never occurs from B.C.G. Ampules of the vaccine as given at Lubeck were grown on boullion and the green color occurred. Cultures from autopsy material also turned green, so it was the Kiel culture used by mistake that caused the deaths and not B.C.G., for as stated B.C.G. does not produce the green color. The court so decided and declared B.C.G. blameless.

When Calmette died in 1933, the use of B.C.G. was practically discontinued. The Scandinavian countries, however, as well as some others, retained their faith in Calmette and continued its use. Gradually it was started again elsewhere. Not one report of untoward results or suggested virulence has been reported in the last twenty years. It is now accepted in most of the countries of the world. The worry today is not that the use of the vaccine is hazardous, but rather that it might not be virulent enough to cause sufficient resistance and immunity to tuberculosis. In one instance 400 times and in another 2,000 times the usual dose was given by accident with no ill effects. The liquid form loses some of its potency if too long a delay occurs between its manufacture and its use. Dry vaccine can be transported with less need for haste.

B.C.G. is just now coming into its own. The numbers of controlled vaccinations in each country, however, are naturally relatively small. In all groups, however, the morbidity and mortality rates were markedly reduced and no complications followed its use.

In India I was told by both Dr. Benjamin, Tuberculosis Adviser to the Government of India, and Dr. Mani of the World Health Organization in Delhi that because of the lethargy of the United States and England regarding its use the doctors are skeptical of its efficacy and its popularity in India has been seriously retarded.

In Japan the mortality rate, in 1945, was 289 per hundred thousand. In that country as in others vaccination is now compulsory. Under General MacArthur and Brigadier General Sams the mortality rate has been markedly reduced. Thirty-one million B.C.G. vaccinations have been given there with not one untoward result. In the vaccinated group the reduction in mortality has been 88 per cent. This was done under the badly overcrowded and unhygienic conditions.

In Copenhagen B.C.G. vaccination has been carried on since 1927, but its use was carried on slowly and with great care. At first various small groups were vaccinated with proper controls, etc., but in 1947, mass vaccination was begun. Three hundred thousand vaccinations have been done to date, 150,000 of which were in the last two years. Statistics for large groups therefore are not yet available. In the well-controlled groups, however, some startling figures can be obtained. The most striking of these was in an underground shelter in a Jutland school where by chance the most favorable conditions for evaluating B.C.G. were present. There were three groups of children; 105 of whom had positive reactions from contact, 106 were positive by vaccination, and 94 tuberculin negative and not vaccinated. They were all underground, no light, no ventilation, the same food, etc., and had as a teacher a person with active tuberculosis. An epidemic of tuberculosis broke out and a check-up revealed that in the 105 children positive from contact 4 developed tuberculosis. In the 106 positive by vaccination 2 developed mild tuberculosis. In the tuberculin negative group of 94 not vaccinated, 70 developed tuberculosis. Dr. Tonderlund in Copenhagen stated that vaccination will cause an immunity in 70 to 90 per cent and will last from 4½ to 5 years. If tuberculosis does develop in those vaccinated, it is usually of a milder form. They have found also that patients with positive tuberculin reaction from contact develop tuberculosis 8 to 1 over those positive from vaccination. This is because many contact positives already have active disease which will show up later. This will not be true in a controlled vaccinated group.

It is impossible to dwell at length on the results of the large number of persons vaccinated throughout the world, but I shall give you just a brief summary of some of them. They are, of course, all in well-controlled groups.

In Sweden about 500,000 persons have been vaccinated. In 1945, Anderson and Belfrage reported vaccination of 10.6 per cent of the population of Gothenberg, Sweden, where the mortality as a whole was 68 per hundred thousand, but no deaths from tuberculosis occurred in the vaccinated groups.

In Orebro, Sweden, Malmos reported 22,413 vaccinations with no deaths in the vaccinated group, and only one case of tuberculosis developing in those vaccinated.

In Bores, in the same country, Torwell reported 19,000 vaccinations by 1947, and the mortality rate was 1 to 19 in the vaccinated group as compared to those not vaccinated.

In Norway, more than 400,000 vaccinations have been done. Heinbeck reported that in controlled groups the morbidity and mortality in the vaccinated persons was from one-fifth to one-tenth in the nonvaccinated. This was after 23 observation years.

In Bergen none of the persons vaccinated between 1937 and 1946 died of tuberculosis although the mortality of the city was 78 per hundred thousand.

In Brazil 164,000 were vaccinated in Rio de Janiero alone up to 1946. Orlando de Assis stated that the number of deaths in the newborn infants living in tuberculous families varies from 8 to 30 per cent. In the vaccinated groups it was 2.2 per cent.

In Argentina 500,000 vaccinations were done and Gomez reported the mortality in the vaccinated group was one-sixth of those not vaccinated.

In Russia millions of vaccinations have been reported and great claims are made of the results, but as no one believes the Russians anyway, and because I was refused permission to enter the country to observe their work, I shall omit their figures.

In Uruguay over 200,000 vaccinations have been done and the mortality rate is five to six times higher in nonvaccinated than in the vaccinated controls.

In Columbia 26,800 were vaccinated up to 1948. In one group the morbidity was 1.1 per cent in vaccinated group and 15.1 per cent in the nonvaccinated group.

In France 2,000,000 persons were vaccinated up to 1948. All report decreased mortality in vaccinated groups.

In Greece 34,279 were vaccinated in Athens and Pireus. In one control group no deaths from tuberculosis occurred in those vaccinated while 10 per cent died in the nonvaccinated.

In Algeria they vaccinate everyone every three years without taking tuberculin tests. In all these vaccinations as with all the 50 million now given there were no ill effects following its use.

The surprising thing is that B.C.G. is not used more extensively in the United States for it is in this country where some of the most competent and experienced bacteriologists and investigators of B.C.G. are working, and where some of the most carefully supervised experiments on its efficacy and harmlessness were undertaken. The most important of these studies were made by Aronson and Palmer, Park, Rosenthal and Birkhaug.

Dr. Park, of New York, reported 690 vaccinated and 755 controls all hailing from tuberculous families, carefully analyzed and followed for ten years. The mortality rate was one-fourth as high in those vaccinated as in the controls. Dr. Camille Cayley, who worked with Dr. Park for twenty-three years, stated that when Park died he was convinced that analysis of small groups would not properly demonstrate the effectiveness of B.C.G. and advised mass vaccination.

Aronson and Palmer made a study of B.C.G. on the North American Indians beginning in 1936. There were 1,551 vaccinated and 1,457 controls. They were followed for eleven years. There was about 80 per cent reduction in the mortality rate in those vaccinated. Aronson now directs a B.C.G. laboratory at Phipps Institute in Philadelphia.

In Chicago under Dr. Rosenthal a rigidly controlled program was conducted in several groups. Two of these have been observed for thirteen years. *First:* Newborn infants living in areas where the mortality from tuberculosis was up to 300 per hundred thousand. *Second:* Newborn infants in which tuberculosis was present in the household. The mortality and morbidity were reduced in all groups. In Group 1 there were seven times as many deaths in the control group as in those vaccinated. In Group 2 there were no deaths in the vaccinated group and four in the control group. Rosenthal now manufactures B.C.G. at the Tice Laboratory in Chicago under The Research Foundation, which graciously supplies it to many states, including Michigan.

Dr. Konrad Birkhaug directs a B.C.G. laboratory at Albany, N. Y., which furnishes B.C.G. for all New York state. He formerly directed a laboratory at Bergen, Norway, for ten years. He stated that vaccination confers approximately 80 per cent protection against tuberculosis and is absolutely essential to tuberculosis eradication.

These laboratories could furnish a safe vaccine for all the United States. Its indiscriminate manufacture and use cannot be condoned.

It is, of course, understandable that many countries should have been reluctant to embark on a program of vaccination while so much controversy was going on, but now that B.C.G. has been universally accepted as absolutely harmless and does confer immunity up to 90 per cent or over, there can no longer be any valid reason for it being withheld. Limited experiments are no longer necessary.

Vaccinations should begin at birth in every country of the world. When individuals again become tuberculin negative they must be revaccinated and the process kept up throughout their lives, giving some meaning to the shopworn expression "from the cradle to the grave."

The United Nations, the United Nations International Childrens Emergency Fund, World Health Organization, International Congress on B.C.G., the American Trudeau Society, etc., have all sanctioned the use of B.C.G., but we with our ostrichlike attitude and restrictions on its use are retarding its effectiveness. Our United States Public Health Service, who must know the world-wide effectiveness and harmlessness of B.C.G. for the last twenty years, still wishes us to continue experimental work on a small scale. They recommend that it be used first on doctors, nurses, and hospital employees, and in areas where tuberculosis is most prevalent. Obviously they consider it harmless and effective, for otherwise they could not suggest that their colleagues, nor any group, be used as guinea pigs. It is certain that with its use some person in contact with tuberculosis will develop the disease before vaccination has time to become effective. This event might erroneously be blamed on B.C.G. and is likely to induce timidity in official circles.

We spend billions to avert wars and billions to fight them, yet the suffering and loss of life from these conflicts are infinitesimal compared to the ravages of this disease for which we do so little. Tuberculosis is not being eradicated any place in the world. Let us have the honesty to accept the futility of our present methods alone, and the courage to embark immediately on a program of extensive B.C.G. vaccination, without which, tuberculosis will present the same problems a thousand years from now as it does today.

INTRATHORACIC NEUROGENIC TUMORS

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THE intrathoracic tumors originating in nervous tissue constitute a comparatively well-defined group. Their typical site is in the posterior mediastinum, and furthermore, they have fairly typical shape. Because of their site they often give rise to no symptoms until they have reached a considerable size, and therefore, they are not infrequently found accidentally during a routine chest examination. As a result of their slow growth and few clinical symptoms they have often been considered purely benign, and since the mortality for surgical treatment is about fifteen per cent in the literature, the principles underlying the treatment of these tumors have been poorly defined. In considering indications for operative treatment there must be a certain relation between the risk of the operative procedure involved and the patient's prognosis without operative treatment. We know, furthermore, that in general where neurogenic tumors are concerned an operation which is not definitely radical can incite the tumor to malignant transformation.

There has also been a difference of opinion as to the point of origin of these tumors. The thorax contains both cerebrospinal and autonomic nerves. Any of these may be the primary site of these tumors. Most of the neurogenic tumors originate in the intercostal nerves, and it is now a general agreement that the nerve sheath is the primary site. However the problem of whether they originate in the sheath's ectodermal component, the Schwann cells (Verrocay, Masson), or from its mesodermal connective tissue component is not settled (Bailey, Penfield). Efforts to trace the tumors' origin to one of these anatomic structures have resulted in a confusing number of different names. Here the term neurinoma will be used.

Another group of intrathoracic neurogenic tumors whose origin is in the autonomic nerve tissue is the so-called ganglioneuroma. Well-developed ganglion cells are found in these tumors. There may be mixed forms, so that some parts of the tumor have the appearance of a clear picture of neurinoma. In spite of this there is pathologic anatomic cause to separate these two groups. In our material there is only one single case of ganglioneuroma (Case 16).

Kent and associates (1944) collected 105 cases of intrathoracic neurogenic tumors from the literature and found a 37 per cent frequency of malignancy. In their own study of 19 cases from the Barnes Hospital they found 41 per cent malignancy. If they followed a topographic grouping of their cases, namely those situated in the mediastinum and those tumors situated anterior in the chest wall, they found that the latter showed a greater percentage of malignancy, 88.8 per cent, while the true tumors of the mediastinum were malignant in 20.3 per cent of the cases.

From the Surgical University Clinic A.

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Blades (1946) found in his study of 29 tumors that only 1 was clinically and histologically malignant. We shall return later to these conflicting statistics.

The diagnosis of these tumors is made chiefly by x-ray examination. The appearance is a clear-cut, sharply outlined, nonpulsating tumor mass with a base located against the mediastinum or spinal column. When there is a "dumbbell" tumor, special roentgenograms will show widening of the intervertebral foramina. In the same manner, most often in cases of malignancy, defects in the adjacent ribs or vertebra may occasionally be seen. However, this may also occur as result of purely mechanical pressure, particularly when the tumor is located in the superior sulcus, so it is not a certain symptom of malignancy. Exudative reaction in the pleura, even hemorrhagic, is not a definite sign of malignancy (Harrington). Intrathoracic neurinoma in connection with von Recklinghausen neurofibromatosis is often malignant (Ewing).

MATERIAL AND METHODS

At the University Hospital, Oslo, Surgical Clinic A, in the period from 1933 to 1947, 21 cases of intrathoracic neurogenic tumor have been treated.

There were 11 women and 10 men varying in age from 21 to 59 years (Table I). There are comparatively many in the age group from 20 to 30 years, while the remainder are evenly distributed in the group from 30 to 60 years.

In 12 of the patients the disease was accidentally discovered during a [illegible]outine chest examination. The other 9 went to the doctor for symptoms which [illegible]d to a special examination of the lungs. These symptoms were as follows: dyspnea in 2 cases, pain in the affected side of the chest in 5 cases, palpable tumor on the anterior chest wall in 1 case. In 2 cases in which the tumor was located in the superior sulcus a Horner's syndrome and pain in the shoulder and arm with paralysis and atrophy were present. This Pancoast syndrome should be borne in mind in all stubborn cases of neuralgia of the shoulder area. The neuralgia often precedes the full development of Horner's syndrome.

The diagnosis of neurinoma or probable neurinoma was made in 17 cases on the basis of roentgenograms. In one case a diagnosis of mediastinal tumor was made, but it was impossible to classify the tumor further. One case (Case 16) diagnosed as tumor of the lung will be discussed later. In one case (Case 18) there was a coincidental syphilitic infection, so that the possibility of a syphilitic process in the chest was discussed. The tumor mass remained unchanged after antisyphilitic treatment, and since it had the typical appearance of neurinoma, the patient was operated upon and this diagnosis verified. As is seen from the foregoing, the roentgenologic diagnosis is relatively certain, at least in the case in which the tumor has a typical site (Figs. 1 to 5). In some cases of dermoid cysts of the mediastinum the differential diagnosis can be difficult (Fig. 6). Most of the tumors were localized in the upper posterior mediastinum. In two cases (Cases 2 and 21) the tumor was localized on the anterior chest wall. These tumors were malignant, and one of them recurred

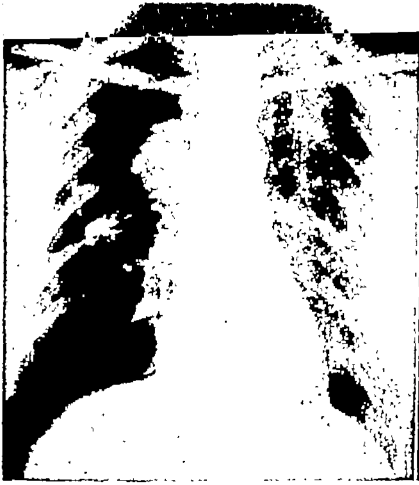

Fig. 1.

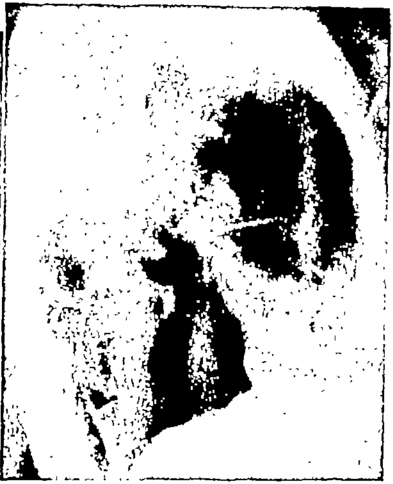

Fig. 2.

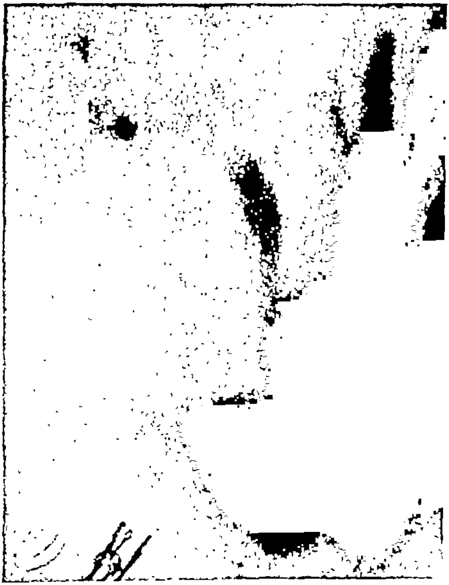

Fig. 3.

Figs. 1, 2, and 3.—A typical neurinoma of the fifth intercostal nerve. The planigram shows its base pointing against the mediastinum.

TABLE

NO.	SEX	AGE	OPERATION (YR.)	SYMPTOMS	SITE	SIZE	PALISADE	CELL NUMBER	NUCLEUS
1	M	35	1946	–	Posterior mediastinum (IX i.c.n.s.)*	Grapefruit	+	Moderate	Moderate hyperchromatic
2	M	28	1945 1946 1947	Neuralgic pain	Anterior lateral chest wall	Orange	+	Varying	Moderate hyperchromatic
3	F	50	1946	–	Posterior mediastinum (VI i.c.n.d.)†	Orange	+	Moderate	Moderate hyperchromatic
4	M	25	1946	Superior sulcus syndrome	Superior sulcus	Orange	+	Large	Marked atypical
5	F	23	1938	–	Posterior mediastinum	Egg	+	Varying	Normal
6	F	48	1945	–	Posterior mediastinum (V i.c.n.d.)	Egg	+	Varying	Normal
7	F	28	1947	–	Posterior mediastinum (VIII i.c. n.d.)	Pigeon egg	+	Small	Normal
8	M	41	1945	–	Posterior mediastinum (V i.c.n.d.)	Orange	+	Moderate	Normal
[illegible]	F	33	1933	Dyspnea	Posterior mediastinum (VII i.c.n.s.)	Pigeon egg	+	Moderate	Normal
[illegible]	M	48	1939	–	Posterior mediastinum (VII i.c.n.s.)	Orange	+	Moderate	Normal
1	M	54	1945	–	Posterior mediastinum (VI i.c.n.d.)	Grapefruit	+	Moderate	Normal
2	M	22	1947	–	Posterior mediastinum (IX i.c.n.s.)	Orange	+	Moderate	Normal
13	F	24	1943	Superior sulcus syndrome (von Recklinghausen's disease)	Superior sulcus	Grapefruit	+	Large	Marked atypical
14	F	44	1946	–	Posterior mediastinum (IV i.c.n.s.)	Egg	+	Small	Normal
15	F	21	1939	Pain	Posterior mediastinum (III i.c.n.s.)	Pigeon egg	+	Small	Normal
16	M	35	1946	–	Interlobar, near recurrent nerve	Egg	-	Varying	Moderate hyperchromatic
17	F	52	1948		(II i.c.n.s.)	Grapefruit	+	Varying	Normal
18	M	29	1945	Pain	(V i.c.n.d.)	Orange	+	Moderate	Normal
19	F	52	1947	Pain	Vagus nerve	Grapefruit	+	Small	Normal
20	M	60	1947	Pain	Anterior lateral chest wall	Orange	+	Varying	Marked atypical
21	F	59	None	Dyspnea	Posterior mediastinum	Orange	+		

*Left intercostal nerve.

†Right intercostal nerve.

HISTOLOGIC FINDINGS MITOSES	FIBROSIS	MYXOMATOSIS	XANTHOMATOUS CELLS	LEUCOCYTES	INVASIVE GROWTH	HISTOLOGIC DIAGNOSIS	COURSE
-	+	+	-	-	-	Semimalignant	No recurrence
Few	sl. +	+	-	+	+	Malignant	Recurrence
-	sl. +	+	-	+	-	Semimalignant	No recurrence
Some	sl. +	+	-	-	+	Malignant	Dead postoperatively
-	++	-	+	-	-	Benign	No recurrence
-	++	+	-	+	-	Benign	No recurrence
-	++	+	-	+	-	Benign	No recurrence
-	+	++ (cysts)	+	+	-	Benign	Dead postoperatively
-	+	+	-	-	-	Benign	No recurrence
-	+	+	+	+	-	Benign	No recurrence
-	+	++ (cysts)	-	-	-	Benign	No recurrence
-	+	-	+	-	-	Benign	No recurrence
+	+	+	+	-	-	Malignant	Recurrence Dead
-	+ (calcified)	-	-	+	-	Benign	No recurrence
-	+	-	-	-	-	Benign	No recurrence
-	-	+ (cysts)	+	-	-	Semimalignant	No recurrence
-	+	-	-	+	-	Benign	No recurrence
-	+	+	-	-	-	Benign	No recurrence
-	++	-	-	-	-	Benign	No recurrence
Some	+	+ (cysts)	-	+	+ (II rib)	Malignant	Short observation time Unchanged, 2 yr. observation time

after a short time. One tumor (Case 16) was situated near the hilus of the lung between the upper and lower lobes, so that the possibility of a primary neurinoma with origin in the lung itself was discussed, though this is a very rare condition (Barlett and Adam). During the operation it was evident that the neurinoma had its origin in the recurrent nerve and the patient showed postoperatively signs of paralysis of this nerve. Blades and Dugan have reported a case of neurinoma of vagus origin. One of our patients (Case 19) also had a neurinoma of probable vagus origin. The rest had their origin in the intercostal nerves.

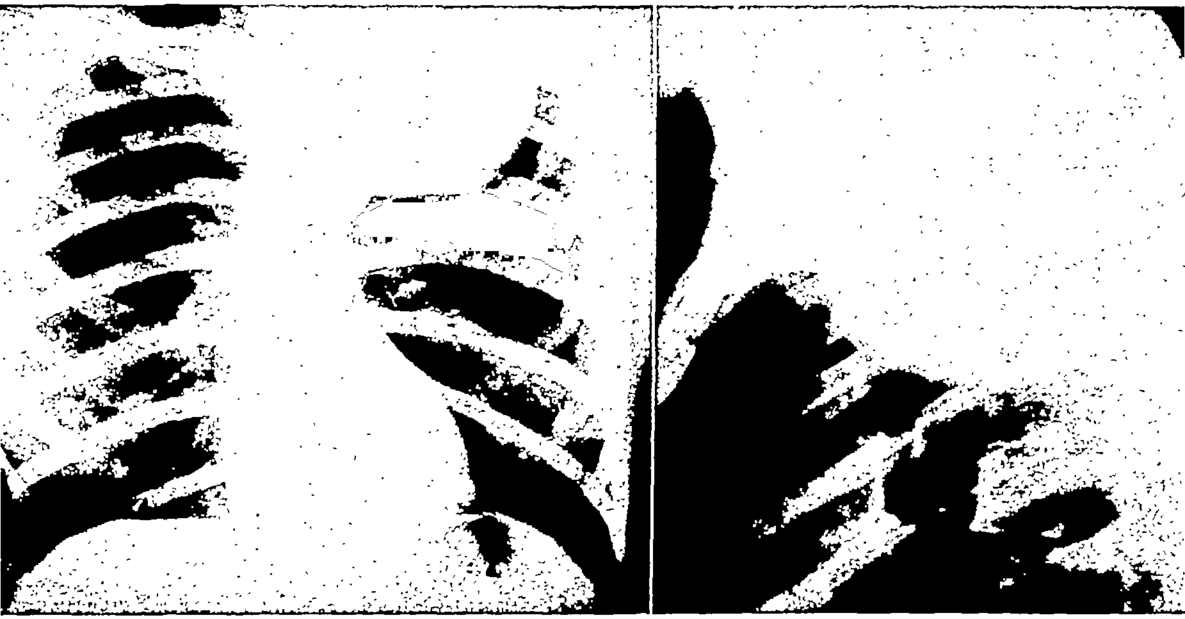

Fig. 4. Fig. 5.

Figs. 4 and 5.—Neurinoma localized in the superior sulcus producing the Pancoast syndrome.

The treatment was operative in 20 cases. In some cases we attempted a paravertebral, extrapleural approach. However, the tumor was so intimately attached to the pleura that a lesion of pleura resulted in all cases except one. This experience led to the use of the usual transpleural dorsolateral thoracotomy incision in all our later cases, as it gives a much more satisfactory exposure.

There were 2 postoperative deaths (Cases 4 and 8): One patient died the day after the operation without having recovered consciousnss. It was considered as a result of anesthesia. Post-mortem examination revealed degenerative changes in the cerebrum. Th other patient died four days postoperatively with a hyperpyrexia. Chemotherapy had no effect. In post-mortem examination nothing was found to explain the hyperpyrexia or the immediate cause of death.

Other complications were two postoperative empyemas which had to be drained. One of these developed first a typical clotted hemothorax which was secondarily infected. The possibility of performing decortication to produce expansion of the lung was discussed. Later x-ray examination revealed full expansion of the lung. The others all developed a postoperative hemorrhagic exudate which was aspirated. It was occasionally difficult during the operation before the time of absorbable hemostatic agents to get complete hemostasis in the tumor bed. This is possibly the reason for the not infrequent marked postoperative temperature reaction observed in this material. Follow-up examinations showed, however, that the lung had completely expanded in all cases.

Thrombosis occurred once. Paralysis of the recurrent nerve once. As mentioned before this may have been due to origination of the tumor in the recurrent nerve. One patient died a few months after the operation, as result of recurrence of the tumor. One patient developed recurrence in the course of a few months. His tumor was located in the anterior chest wall. Microscopic examination revealed malignant neurinoma both in the primary and the recurrent tumor. None of the remainder of the patients showed any sign of recurrence at follow-up examination. It is evident from this examination that the postoperative prognosis is good in all cases in which the primary lesion was a benign neurinoma. Even the cases (Cases 1, 3, and 16) in which the histologic examination showed some signs of atypical growth, remained symptom free. Therefore this study does not support the view held by some that these patients should not be operated upon because of the danger of recurrence. The same conclusion may be drawn from Makka's study.

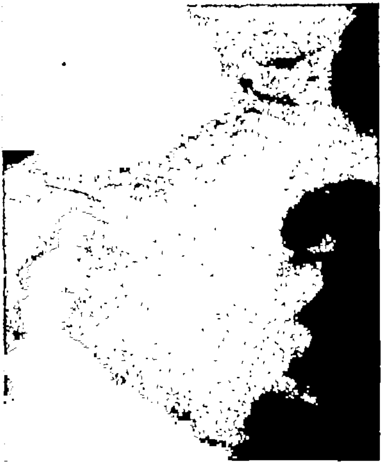

Fig. 6.—Dermoid cyst in the upper mediastinum.

In this material there were 2 postoperative deaths. One death (Case 4) occurred in a patient with a malignant Pancoast tumor; in this case there were obvious indications for operation. The other death (Case 8) occurred in a pa-more both cases in this study (Cases 4 and 13) with localization in the superior sulcus were malignant. These tumors also are in a special group, because they give early pressure symptoms and present considerable difficulty for radical extirpation. The size of the tumors in this material did not give any definite prognostic data though none of the small tumors were malignant. As a whole it appears that there are no definite clinical criteria for possible malignancy. Puncture biopsy is not decisive, except in those cases in which it gives a definite answer of malignancy. An added factor is that the malignant tumors have a poor prognosis, no matter what the treatment, so the advantageous period for surgical treatment is gone.

As to the second problem it is difficult to judge the benign tumors' tendency to undergo malignant transformation because there is no unoperated material that has been observed over a sufficiently long period. Therefore we have only the frequence of malignancy as an index, and it varies markedly in the different material reported, as mentioned earlier. Thus in Kent's own study and in his collected study, the frequency is high, 41 and 37 per cent, while in Blades' study and this study, where a larger number of the patients had tumors accidentally discovered, the frequency is lower. If the tumors in this study are divided into two groups, those which produced symptoms and those discovered accidentally, the frequency of malignancy is 4 of 9 and 0 of 11, in that order. Even though it is presumed that many patients can live long with intrathoracic neurinoma, these figures should indicate that the tumors have so marked a tendency to malignant transformation that the only effective method of treatment, radical surgical extirpation, is indicated. Although the operative mortality is high in the cases operated on some time ago, it may be expected that it will be greatly reduced by the recent progress in chest surgery. Another factor which will reduce the operative mortality is that by early operation the percentage of benign tumors is greater and therefore the operative risk less.

SUMMARY

1. This is a review of 21 intrathoracic neurogenic tumors, 20 of which were treated surgically, 12 were discovered accidentally, 9 presented clinical symptoms. Those discovered accidentally were all benign. Four of those which presented symptoms were malignant, 2 of them were localized in the superior sulcus, and 2 in the lateral chest wall.

2. The difference in frequency of malignancy in the asymptomatic and the symptom-producing groups, together with the histologic findings of a semimalignant group, is evidence that malignant transformation is not infrequent. The fact that none of the small tumors were malignant supports this view.

3. It is only possible to ascertain the number of tumors which will later undergo malignant transformation by observation over a period of years. Where the poor results of treatment of the malignant tumors are compared with the good results of treatment of the benign, the advisability of such an experiment is doubtful.

4. Every diagnosed intrathoracic neurogenic tumor must be considered potentially malignant and should be treated surgically.

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TRANSTHORACIC APPROACH FOR COMPLETE REMOVAL OF THE POSTERIOR MEDIASTINAL AND INTRAVERTEBRAL PERINEURAL FIBROBLASTOMA

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TUMORS arising from nerve sheaths and growing both in the intravertebral canal and posterior mediastinum are generally described as dumbbell or hourglass tumors. Usually these tumors have been removed by separate surgical attacks upon their component parts. Those small tumors which have extended from the intravertebral canal into the paravertebral region have not infrequently been removed through the usual laminectomy incision and resection of the transverse processes of the vertebrae and the articular ends of one or more ribs (Heuer,[1] Naffziger,[2] Alessandri,[3] Craig[4]). The massive posterior mediastinal extensions from the intravertebral canal would pose a dangerous and generally impossible technical problem for a one-stage removal through the usual laminectomy approach. For these latter tumors, a two-stage procedure was devised. Harrington and Craig[5] reported a successful removal of a dumbbell tumor which grew primarily in the mediastinum combining bilateral laminectomy and thoracotomy through separate incisions. With the experience we gained from the following patient, it is our purpose to describe a somewhat different approach for the one-stage removal of these large hourglass tumors because we believe the procedure greatly simplifies the technical problem.

CASE REPORT

Historical Data.—E. B. (Case 172994), a white girl, aged 17 years, was admitted to the Graduate Hospital on May 6, 1947, complaining of weakness and numbness of the legs and inability to void. She was perfectly well up to three years before admission to the hospital when she developed pain in the right shoulder and scapular area. This pain radiated into the right arm. It was both burning and knifelike in character and continued almost constantly for a period of two years when it lessened considerably. One year before admission the patient noticed weakness of the legs which slowly progressed so that she had great difficulty in walking. About three weeks before admission to the hospital, numbness and tingling developed in both legs, right more than the left, and at approximately the same time she noticed difficulty in initiating urination. When admitted to the hospital she required regular catheterization.

The past and family history were irrelevant.

Physical and Neurological Examination.—The patient was a well-developed, thin woman slightly above average height. A detailed physical examination was essentially normal, except for a palpable bladder. The blood urea nitrogen, blood sugar, complete blood count, and urinalysis, except for a few pus cells, were within the normal range.

Neurological examination revealed the cranial nerves and upper extremities to be normal. The lower extremities were definitely weak in all muscle groups and they were

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markedly spastic. Knee and ankle reflexes were increased and there was a bilateral unsustained ankle clonus with a bilateral Babinski reflex. Abdominal reflexes were absent. Sensations of pain and temperature were reduced in patches over the lower extremities and abdomen, suggesting a level at about the eighth thoracic vertebra. Position, touch, and vibratory sense were normal throughout the trunk and lower extremities.

Special Studies.—Lumbar puncture was not done because of studies described below. X-ray films of spine disclosed a sharply demarcated defect involving the lower portion of the body of the second and upper portion of the body of the third thoracic vertebrae on the right (Fig. 1). This bone defect was edged by a line of increased density. Associated with this defect was a soft tissue mass, measuring 5 cm. in diameter, extending into the posterior mediastinum (Fig. 2). The cervical spine showed no abnormalities. The superior and inferior plates of the bodies of the upper lumbar vertebrae were irregular and the first lumbar vertebra appeared to be wedged. This was interpreted as possibly the result of an old, mild osteochondritis.

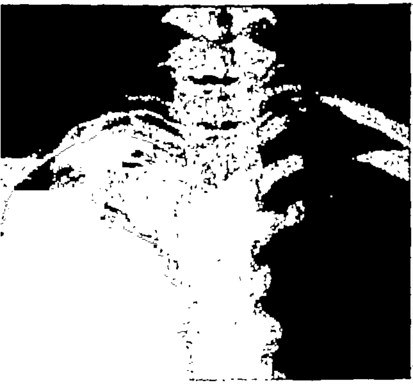

Fig. 1.

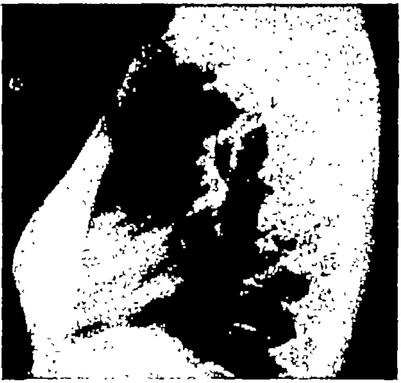

Fig. 2.

Fig. 1.—Roentgenogram of chest and upper thoracic spine showing tumor eroding bodies of second and third thoracic vertebrae.

Fig. 2.—Lateral roentgenogram of chest showing extension of tumor into posterior mediastinum.

As a result of x-ray studies, a diagnosis of a tumor of the posterior mediastinum coming from the intervertebral canal was made. Because of the three year history, a benign, perineural fibroblastoma was suspected. It was felt that the best opportunity for a complete removal in a one-stage procedure was offered by the combined efforts of the thoracic and neurological surgeons.

Operation.—On May 14, 1947, with the patient lying in a full lateral position upon the left side, and under endotracheal ether-oxygen anesthesia, an incision was made beginning 3 cm. below the upper border of the right trapezius muscle, midway between the spine and posterior border of the right scapula, extending downward and curved outward to the auscultatory triangle. The scapula was retracted anteriorly and 10 cm. of the posterior portions of the third, fourth, and fifth ribs were removed subperiosteally down to the transverse processes of the vertebral body. The right pleural cavity was entered, and in the posterior mediastinum to the right of the spinal column, a large, very firm tumor covered with parietal pleura was exposed. The tumor extended over the midline on the anterior border of the body of the third dorsal vertebra. The posterior portion of the tumor was fixed to the vertebral border by dense fibrous tissue. The tumor was freed from the vertebral bodies and retracted to the right, thus revealing the extension through the intervertebral canal. The tumor was about 10 cm. in length and the intrathoracic portion about 5 cm. in diameter. At this point, the neurosurgeon entered the operative team.

The paravertebral muscles were retracted medially, exposing the right laminae of the second, third, and fourth thoracic vertebrae. The tumor from the chest was then mobilized completely and also from the portion of the vertebral bodies to which the tumor was attached. It was clear that the intervertebral foramina between the second and third thoracic vertebrae was markedly enlarged at the point from which the extension of the tumor had occurred. However, the tumor mass involved the roots of the fourth thoracic as well as the second and third. All three roots had to be sectioned in order completely to mobilize the tumor. The right laminae of the second and third thoracic vertebrae were then removed, exposing the intravertebral portion of the tumor which was anterolateral with regard to the dura and spinal cord. The spinal canal portion of the tumor was mobilized without difficulty, and the entire tumor removed. Hemostasis was secured readily. The chest muscles were then repaired in layers by interrupted cotton sutures and a tight closure secured. Neither the pleural cavity or wound were drained.

Postoperative Course.—The patient's postoperative condition was at all times satisfactory. On one occasion, four days postoperatively, 500 c.c. of bloody fluid was removed from the right pleural cavity, but no other thoracentesis was necessary. After consultation with an orthopedic surgeon,* the patient was fitted with a high spinal brace and discharged on the sixteenth postoperative day. The surgeon was of the opinion that the erosion of the second and third thoracic vertebral bodies, together with the hemilaminectomy performed at operation, had so weakened the vertebral column that spinal fusion was indicated. Consequently, the patient returned to the hospital on July 3, 1947, two months after removal of the tumor. A spinal fusion of the first to fourth thoracic vertebrae was performed on July 14, 1947, without difficulty, and the patient was discharged wearing her brace on Aug. 6, 1947. At the time of her final discharge from the hospital, she was asymptomatic neurologically. When last seen on May 25, 1948, she was symptom-free, neurologically negative, and the thoracic spine was quite stable.

Pathology.—The gross description of the pathologic specimen was as follows: The specimen consisted of one large and several small, connected nodules. The entire length of the specimen was 11 cm. The large nodule was 5½ cm. in diameter. The cut surface showed alternating areas of whitish and yellowish tissue. The tissue was firm, elastic but not hard. There were several areas of hemorrhage throughout the specimen.. Microscopically the tissue was composed of streams of nuclei with occasional tendency to palisade formation. The cells appeared to be generally bipolar with long, slender processes lying parallel with each other. Between these bands of tissue there were reticulated areas containing polygonal edematous-appearing cells. These latter areas, however, formed only a small portion of the neoplastic tissue. The tumor was rather vascular and many good-sized vessels were seen throughout. No nerve fibers or any fibers resembling nervous tissue were seen. The microscopic diagnosis was perineural fibroblastoma.

COMMENT

The diagnosis in this patient was made by x-ray films which demonstrated a marked defect of the bodies of the second and third thoracic vertebrae. This finding caused special views to be taken which demonstrated very clearly an intrathoracic tumor. In the diagnosis of these tumors, the most important single examination is x-ray of the spinal column and special views to bring out the soft tissue mass in the chest. The significance of this fact was brought to our attention recently. This patient (Case 183736) was diagnosed as having a primary spinal cord tumor and roentgenograms of the spinal column were not examined critically by the surgeon. A laminectomy was performed and the tumor, a perineural fibroblastoma, was exposed and found to extend into the mediastinum. Laminagraphs were made after this operation and the large mediastinal mass was demonstrated. It was necessary to do a thoracotomy to remove the extension. Had special x-ray films been made prior to the operation of laminectomy, the two-stage procedure would have been avoided.

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*Dr. J. T. Nicholson.

The great size of the intrathoracic growth in the patient being reported made it apparent that the tumor could not be removed completely by the usual *laminectomy operation. Essentially, the planned approach in our patient consisted* of a wide exposure of the mediastinal mass by removal of the overlying ribs, in this instance three, permitting an excellent exposure of the thoracic portion of the tumor which was readily mobilized. It was then quite easy by retraction of the paravertebral muscles medially and posteriorly to do a hemilaminectomy and remove the intraspinal portion of the tumor. Bleeding from the epidural veins was more readily controlled than in a laminectomy approach. The nerve roots to which the tumor was attached could be seen clearly by manipulation of the tumor and consequently easily sectioned.

Further advantages of this approach are: (1) It provided for the complete removal of the tumor under direct vision through one incision. The transpleural approach allows a complete exposure of the larger portion of the tumor. The freeing of the tumor up to the vertebral foramen may then be accomplished without difficulty. Mobilization of this portion of the tumor can be done with least danger to the large vessels of the thorax. (2) It enabled the neurosurgeon to remove the minimum amount of vertebral bone to expose the lesion. (3) The intravertebral extensions of these tumors are generally anterolateral with regard to the dura and spinal cord. This approach provides more adequate exposure of this area than does the classical laminectomy. (4) Since all portions of the tumor are directly visualized, complete removal can be assured.

SUMMARY

A technique for the one-stage removal of the so-called hourglass or dumbbell tumor involving the posterior mediastinum and intravertebral canal is described. It consists of thoracotomy for mobilization of the intrathoracic portion of the tumor combined with hemilaminectomy accomplished through the same incision and by medial retraction of the paravertebral muscles. The intravertebral extension and the narrow isthmus of tumor in the intervertebral canal are thus exposed together with the mediastinal portion, permitting the removal of the tumor in its entirety.

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CHOLESTEROL PERICARDITIS

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CHOLESTEROL pericarditis is an exceedingly rare disease. Only one case (Merrill, 1938[1] has been reported in the English literature. It was first described in the German literature, but only a few cases have been reported in that country.[2] In a Swiss journal in 1941, a case of chronic hemorrhagic pericarditis was described[3] in which the granulomatous epicardium contained numerous collections of cholesterol crystals surrounded by giant cells. Because such clinical entities are rare, we are presenting the following case report.

A 27-year-old opera singer was referred to St. Luke's Hospital on Nov. 13, 1941, complaining of increasing dyspnea and fatigability for two months. Until the onset of these symptoms she had been in excellent health. On admission dyspnea, which had an insidious onset, had progressed to the point where she became out of breath on climbing one flight of stairs. Loss of stamina and weakness on admission were of such degree that the slightest exertion produced profound distress. In the month preceding admission she had had several attacks of ''palpitations'' and had also noticed a sense of heaviness in the left upper chest which was associated with a sharp sticking pain in the region of the left nipple.

Other than the usual uncomplicated childhood diseases the patient had had no significant illnesses in the past.

On physical examination the rectal temperature was 99.2° F., the pulse 86 per minute, and the respiratory rate 18 per minute. The blood pressure was 110/70. The thyroid gland was found to be slightly and diffusely enlarged. The area of cardiac dullness was extensive, extending from 2.5 cm. to the right of the sternum to left posterior axillary line. There was a regular sinus rhythm and the heart sounds were described as distant but of good quality. No murmurs were heard. The liver, firm and nontender, was palpable 3 cm. below the costal margin. The remainder of the physical examination was essentially negative.

Initial laboratory data were as follows:

Urinalysis	negative
Hemoglobin	85 per cent
Red blood cells	4.6 million
White blood cells	11,450, with 64 per cent polymorphonuclear neutrophiles, 27 per cent lymphocytes, 5 per cent monocytes, and 2 per cent eosinophiles
Kline	negative
Urea nitrogen	10.6 mg. per cent
Blood sugar	118 mg. per cent
Total cholesterol	167 mg. per cent
Serum proteins	6.45 Gm.
Albumin	4.35 Gm.
Globulin	2.10 Gm.
Sedimentation rate	9 mm. per hour
Basal metabolism	plus 7 per cent

During the course of first two weeks of this patient's stay in the hospital, various tests were performed to corroborate the clinical impression of pericardial effusion. The initial x-ray examination of the chest with oblique (Fig. 1) views revealed that the cardiac shadow

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was greatly enlarged and globular in shape, extending well posteriorly. The barium-filled esophagus was displaced posteriorly and to the right. Laminagraphic studies showed a homogeneous density throughout, making it impossible to distinguish cardiac shadow from fluid. The initial venous pressure was not remarkable (112 mm. of saline solution), but the circulation times showed moderate elevations—arm to tongue, using calcium gluconate, was twenty seconds; arm to lung, using ether, was thirteen seconds. The vital capacity was reduced (2,000 c.c.). On Nov. 27, 1941, a pericardial aspiration was performed at the left costoxiphoid angle and 140 c.c. of viscid golden-yellow fluid was removed. This fluid was remarkable in that it seemed to hold in suspension an opalescent yellow material. Five days later the aspiration was repeated and 2,200 c.c. were withdrawn. The fluid was found to have a specific gravity of 1.020. Chemical examination revealed the following determinations: total protein, 5.65 Gm.; albumin, 2.1 Gm.; globulin, 3.55 Gm.; nonprotein nitrogen, 20 mg. per cent; total cholesterol, 120 mg. per cent. A direct smear of the material was described as loaded with cholesterol crystals, with occasional phagocytic cells filled with fat globules. Culture yielded no pathogens and guinea pig inoculation was negative. Postaspiration cardiograms showed that the T waves in Leads I and IV had become inverted, but that the R waves in all leads had increased in amplitude.

Fig. 1.—Lateral view of the chest showing enormous distention of the pericardium.

During the second aspiration some air was injected into the pericardial sac and fluoroscopy was performed. At this point it was felt that the diagnosis of pericardial effusion was *not altogether conclusive, but rather that the patient had* a large mediastinal cyst anterior to the pericardium and extending into both thoracic cavities. Because of this diagno-

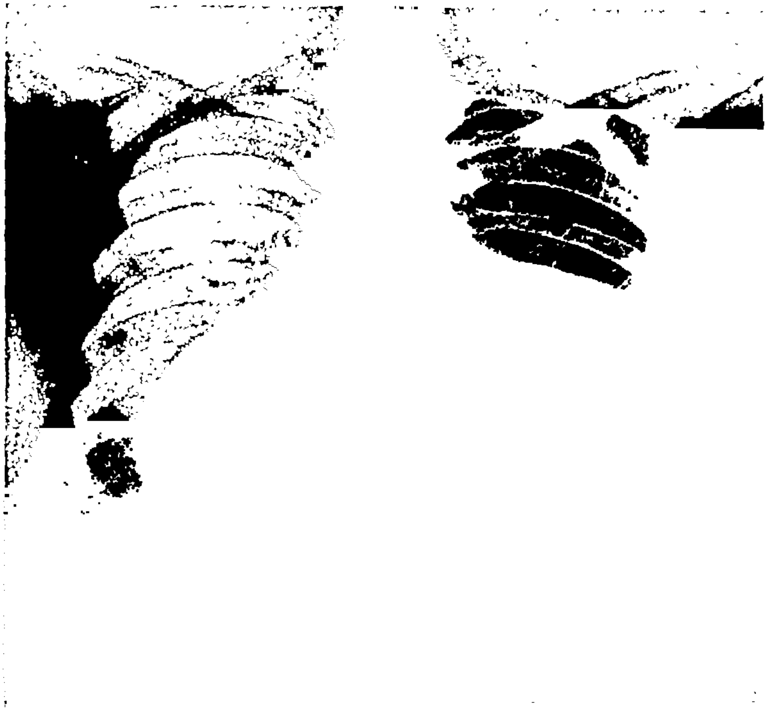

Fig. 2.—Anteroposterior roentgenogram of the chest. Marked enlargement of cardiac shadow.

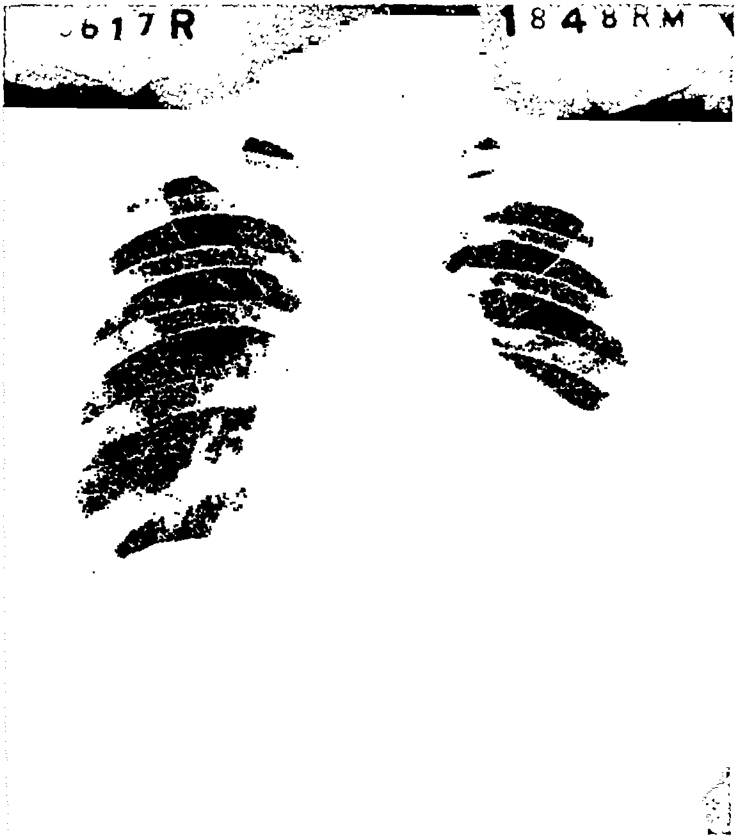

Fig. 3.—Anteroposterior view of the chest seven years postoperatively. Pericardial shadow within normal limits. Patient symptomless.

sis surgical intervention was deemed advisable. On Dec. 23, 1941, a thoracotomy was performed under endotracheal anesthesia. A curved incision was made on the left anterior chest wall and the fourth, fifth, and sixth left ribs, together with the costal cartilage, were removed subperiosteally from the sternum to the midclavicular line. The pericardial sac which was markedly enlarged and slightly thickened contained fluid which at this time was serosanguineous. The parietal pericardium was incised anteriorly and a biopsy was obtained. The fluid was aspirated; it was noted that there were several cholesterol plaques on both the visceral and parietal pericardium. On complete exploration no mediastinal cyst was found. The other structures of the thorax appeared normal. Recovery from the operation was uneventful.

The pathologic report of the section of the pericardium was as follows. Some of the dense hyaline layers of the pericardial sac were recognized, while the lining consisted of granulation tissue with small numbers of inflammatory cells throughout. The mesothelium was very poorly preserved. In other areas, the fibrous layer was mostly replaced by masses of cholesterin and by large numbers of foreign body giant cells and some regenerating fat cells. There was only slight infiltration with polymorphonuclears and lymphocytes. The pathogenesis was not clear but it was possible that it was the result of a pyogenic infection. The pathologic diagnosis was chronic pericarditis.

Bloody fluid was aspirated from the pericardial sac on two occasions following operation. Postoperative roentgenograms of the chest continued to show the presence of fluid in the pericardial space despite aspirations during and subsequent to thoracotomy. Electrocardiographically no significant change was brought about by the operative procedure.

Throughout her postoperative period the patient was relatively asymptomatic. At no time was there any evidence of dyspnea or peripheral edema. Mobilization was begun on the seventeenth postoperative day and she was discharged on the thirty-first postoperative day.

On Feb. 8, 1946, approximately four years later, the patient was again seen at the hospital. At this time she was feeling well and was leading an active life. A chest film taken at this time still showed the heart shadow to be markedly enlarged, relatively unchanged in size since the examination of January, 1942. The roentgenologist stated that from this appearance one could not rule out the presence of fluid in the pericardium. The venous pressure was 157 mm. of saline. Other than a negative T_4 the electrocardiogram revealed no significant abnormalities.

A later follow-up roentgenogram taken Feb. 18, 1948, still showed a somewhat enlarged heart, but no signs of pericardial effusion (Fig. 3).

DISCUSSION

Merrill's case of cholesterol pericarditis had several features in common with the one which we are reporting. Both were women. Both had an effusion fluid containing cholesterol crystals. Merrill's patient had a basal metabolic rate of plus 19 per cent, while our patient had a basal metabolic rate of plus 7 per cent. These values are important in differentiating this condition from the so-called "myxedema heart." Culture of the pericardial fluid was believed contaminated in Merrill's case, negative in ours. Guinea pig inoculation was negative in both. In both the electrocardiogram showed low voltage in all leads.

Significant differences exist, however. Despite the moderately elevated basal metabolic rate, physical examination of Merrill's patient revealed several findings suggestive of hypothyroidism: dry, rough, pale skin; low, husky voice; coarse features; thinning of the lateral portion of her eyebows. Our patient, a large robust opera singer, did not exhibit these features. The blood cholesterol was moderately elevated in Merrill's case (278 mg. per cent), normal in ours (167 mg. per cent). A hypertension of 250/115 existed in Merrill's case, falling

A CLINICAL AND RADIOLOGIC STUDY OF METASTATIC PULMONARY NEOPLASMS

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THE presence in lung of metastases from a primary neoplasm does not always indicate widespread dissemination or justify a resigned and pessimistic attitude. In recent years the resection of pulmonary tissue containing metastases has produced very satisfactory results in certain cases. The present study was undertaken to clarify to some degree the behavior of various types of malignant tumors which metastasize to lung. It is possible that an inquisitive and aggressive attitude toward the clinical progress of malignant disease will enable physicians to select a larger number of patients in whom the surgical removal of pulmonary metastases should be attempted.

The clinical records and chest films of all patients at the University of Michigan Hospital who were reported to show secondary neoplasm of the lungs were reviewed for the five-year period July 1, 1937, to June 30, 1942. When the clinical data were examined, only those cases were retained in which the identity of the primary tumor was established by histopathologic examination, except in the case of several renal tumors which were not approached surgically or at postmortem. In these few instances characteristic pyelographic deformities were accepted as diagnostic. As a background for the 314 cases which were acceptable for study, the total number (5,727) of similar primary neoplasms was determined for the same period. This number (Table I, Column 1) and the number in which pulmonary metastases were discovered roentgenographically (Column 2) are presented for comparison in the table. Some of the first category did not have roentgenograms of the chest made or did not return for a second visit; others doubtless developed pulmonary metastases after their last examination at this hospital, or after June 30, 1942. It should be emphasized because of these factors that no definite conclusions as to the incidence of pulmonary metastases can be drawn from the apposition of such figures. As a matter of fact, due to the care in selection of cases for the study, the actual number of metastases is probably higher than Column 2 would indicate. Nevertheless, a comparison of these figures aids in correcting erroneous impressions of incidence gained from the review of large numbers of metastatic lesions only.

Metastatic involvement of the pleura, as evidenced by the roentgenographic appearance of fluid, was present in 60 patients and mediastinal adenopathy in 53. Of the 77 carcinomas primary in breast, 26, or 33.7 per cent, metastasized to pleura as well as lung and 18 or 23.3 per cent exhibited mediastinal involvement.

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TABLE I. COMPARISON OF THE INCIDENCE OF PULMONARY METASTASES WITH THE INCIDENCE OF PRIMARY MALIGNANT TUMORS OF THE SAME TYPES

	(COLUMN 1) TOTAL NUMBER MALIGNANT NEOPLASMS	(COLUMN 2) NUMBER WHICH METASTASIZED TO LUNG
Carcinoma, breast	907	77
Carcinoma, colon	342	23
Hypernephroma	59	20
Wilms's tumor	11	5
Carcinoma, kidney	17	3
Carcinoma, cervix uteri	777	13
Teratoma, testis	42	14
Carcinoma, testis (seminoma)	8	1
Carcinoma, testis, embryonal	4	1
Chorioepithelioma, testis		3
Carcinoma, bronchus	310	15
Carcinoma, thyroid	65	10
Carcinoma, skin, face	313	1
Upper extremity	60	3
Lower extremity	32	1
Carcinoma, larynx	167	6
Carcinoma, fundus uteri	188	6
Carcinoma, bladder	203	5
Carcinoma, mouth	139	5
Carcinoma, stomach	656	5
Carcinoma, prostate	377	5
Chorioepithelioma, uteri	5	4
Carcinoma, ovary	75	3
Carcinoma, tongue		2
Carcinoma, pancreas	98	1
Carcinoma, lip	373	1
Carcinoma, orbit	1	1
Carcinoma, adrenal	2	1
Carcinoma, pharynx and nasopharynx	46	1
Carcinoma, branchial cleft	2	1
Carcinoma, parotid	40	1
Carcinoma, submaxillary gland	1	1
Sympathoblastoma, adrenal	12	1
Malignant disease, unspecified		
Testicle	1	1
Pelvis	11	1
Uterus	1	1
Adrenal	1	1
Kidney	8	2
Melanoblastoma, skin	36	11
Metastasis lymph nodes	3	2
Metastasis generalized	3	1
Melanoblastoma, eye	29	1
Endothelioma (Ewing's), bones	19	7
Sarcoma, abdomen	7	1
Sarcoma, upper extremity, soft parts	14	9
Sarcoma, lower extremity, soft parts	34	11
Osteogenic sarcoma, bones, lower extremity		8
Osteogenic sarcoma, bones, upper extremity	2	4
Sarcoma, head, soft parts	4	2
Sarcoma (osteogenic), bones, head		2
Sarcoma, breast	3	2
Sarcoma, liver		1
Sarcoma, thorax	7	1
Sarcoma, vulva	1	1
Sarcoma, cervix uteri	2	1
Sarcoma, fundus uteri	5	1
Sarcoma, testis	4	1
Total	5,727	314

These figures are significantly higher than the total number of pleural effusions or mediastinal lesions produced by any other primary malignant lesion in this series.

Of 294 patients about whom information was available on the presence or absence of symptoms, 117 had none which could be ascribed to pulmonary metastases. The distribution of manifestations among the remaining 172 is shown in Table II.

TABLE II. DISTRIBUTION OF MANIFESTATIONS OF PULMONARY METASTASES IN 172 PATIENTS

Cough	129
Dyspnea	75
Sputum	70
Pleuritic pain	51
Hemoptysis or bloody sputum	46
Loss of weight	15
Fever	15
Weakness	14
Fatigue	13
Anorexia	10
Wheezing	6
Night sweats	4
Expectoration of tissue	4
Cyanosis	3
Osteoarthropathy	1

It is surprising how variable the symptoms associated with pulmonary metastasis may be. Miliary or lymphangitic carcinosis is often characterized by a hacking, ineffectual cough and by rapidly progressive dyspnea and cyanosis. However, nodular lesions may be numerous and large without producing respiratory symptoms. Some nodular lesions do produce local symptoms, perhaps by rapid growth and pressure upon or even eruption into a neighboring bronchus. An irritative cough is the commonest symptom. The cough is often nonproductive or at most raises scanty, mucoid sputum, occasionally streaked with blood. The sputum may become purulent if infection arises distal to a bronchial obstruction, or if the necrotic central portion of a nodule is evacuated through a bronchus. In the latter case the resulting cavity is likely to have a very thick wall, so that it looks not unlike a doughnut in the film (see Fig. 1). In at least four patients of this series who had nodular pulmonary metastases there was evidence of cavitation. In one of these patients six nodules which had cavitated were distributed in both lungs. On rare occasions the pathologist may be able to determine the type of neoplasm from bronchial biopsy or from pieces of malignant tissue which the patient has expectorated. It should be possible to identify malignant cells in a much higher proportion of cases by the use of the Papanicolaou technique.

An attempt was made to classify pulmonary metastases by their radiographic appearance into five groups: nodular (see Figs. 2 and 3), which includes the majority; amorphous or infiltrative (see Fig. 4); lymphangitic (see Fig. 5); miliary (see Figs. 6 and 7); and massive consolidation. A clear-cut decision cannot always be made, especially between finely nodular and miliary lesions, or between the miliary and the lymphangitic type. Many lesions could

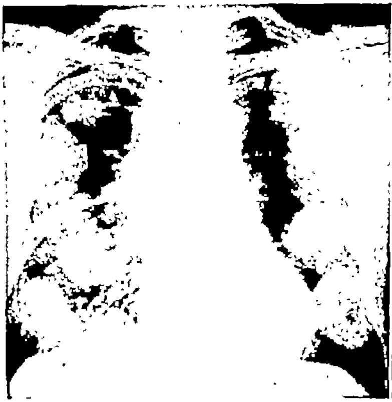

Fig. 1.

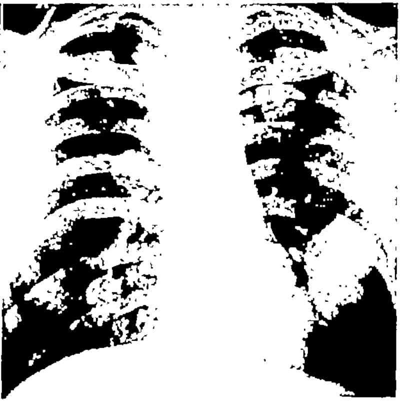

Fig. 2.

Fig. 1.—R. W. (No. 526072), 47-year-old man. Multiple nodules bilaterally. The most inferior one in the lateral portion of the left lower lobe has undergone cavitation. Primary: medullary carcinoma of bladder. Diagnosis primary: May 22, 1943. Diagnosis pulmonary metastases: roentgenogram Sept. 15, 1943, made because of pleuritic pain. Death: Oct. 25, 1943.

Fig. 2.—E. M. (No. 440008), 31-year-old man. Nodular metastases bilaterally. Primary: embryonal carcinoma left testis. Diagnosis primary: Jan. 9, 1939. Diagnosis pulmonary metastases: routine roentgenogram March 20, 1939. No pulmonary symptoms. Death: May 24, 1939.

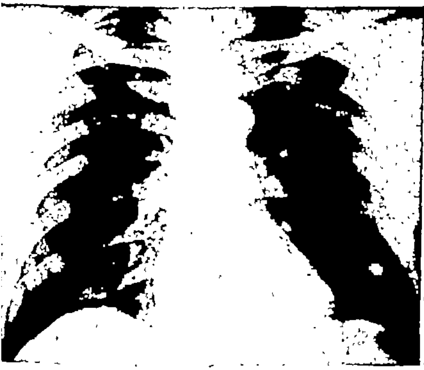

Fig. 3.

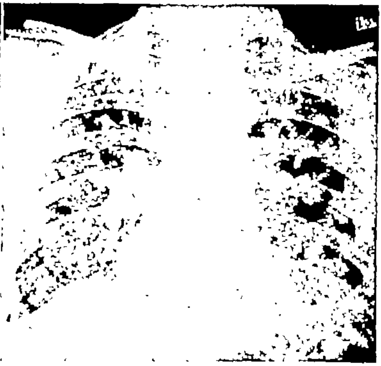

Fig. 4.

Fig. 3.—O. M. (No. 378280), 52-year-old man. Single metastatic nodule in left lower lobe. Primary: adenocarcinoma of sigmoid colon. Diagnosis primary: June 6, 1940. Diagnosis pulmonary metastasis: routine roentgenogram Sept. 12, 1941. No symptoms. Death: Oct. 18, 1941.

Fig. 4.—F. C. (No. 443438), 74-year-old man. Amorphous or infiltrative pulmonary metastases. Primary: carcinoma of the larynx. Diagnosis primary: May 17, 1939. Diagnosis pulmonary metastases: first positive roentgenogram May 17, 1939. No pulmonary symptoms. Death: May 29, 1939.

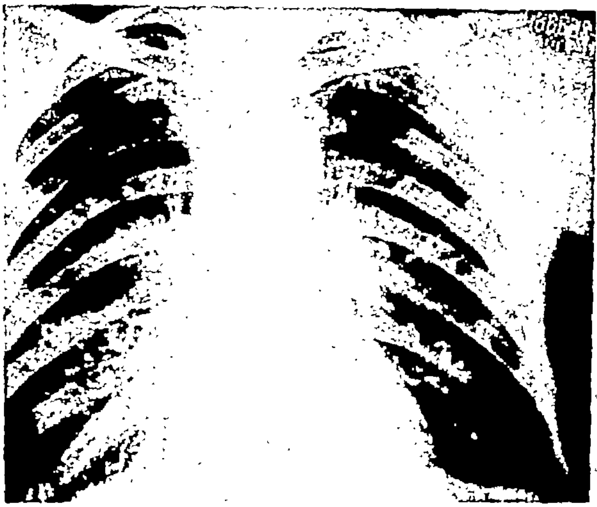

Fig. 5.

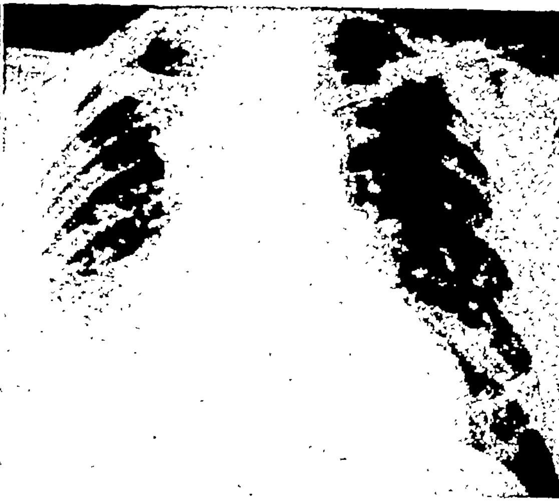

Fig. 6.

Fig. 5.—J. K. (No. 487714), 59-year-old man. Lymphangitic pulmonary carcinosis. Primary: carcinoma of tonsil. Diagnosis primary: August, 1940. Diagnosis pulmonary metastases: roentgenogram Aug. 21, 1941. No pulmonary symptoms. Death: Sept. 2, 1941.

Fig. 6.—C. E. (No. 490721), 69-year-old man. Miliary metastases, paralysis of right hemidiaphragm. Primary: bronchiogenic carcinoma, right. Diagnosis primary: Oct. 3, 1941. Diagnosis pulmonary metastases: roentgenogram Sept. 4, 1941. Symptoms largely those of the primary. Death: Nov. 22, 1941.

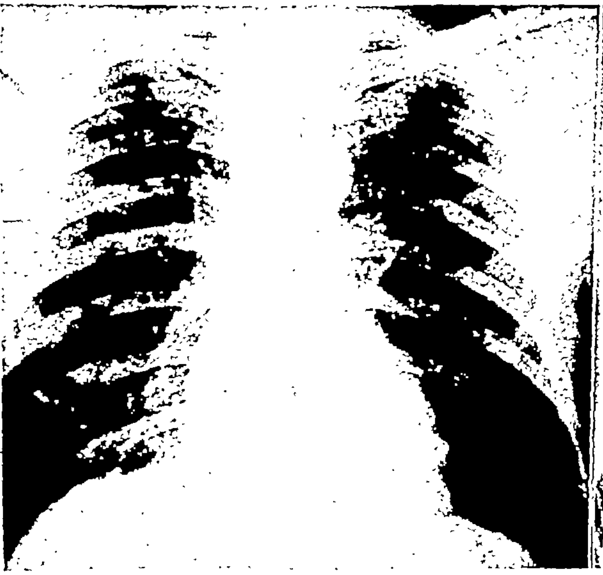

Fig. 7.

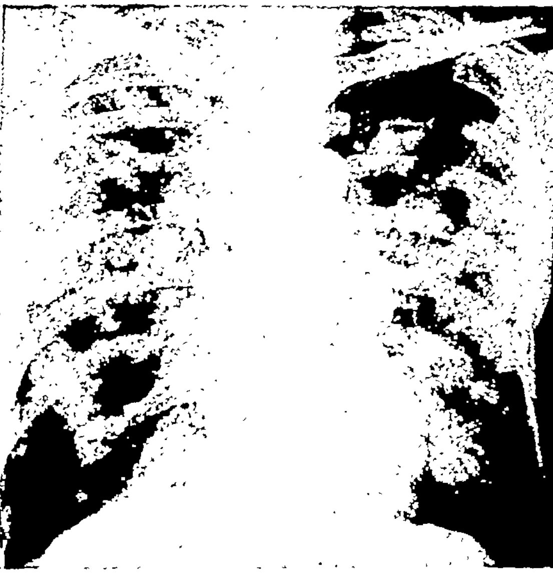

Fig. 8.

Fig. 7.—W. F. (No. 487283), 60-year-old man. Miliary metastases. Primary: adenocarcinoma of bladder and prostate. Diagnosis primary: Aug. 19, 1941. Diagnosis pulmonary metastases: roentgenogram Aug. 30, 1941. No symptoms. Death: Sept. 30, 1943.

Fig. 8.—C. C. (No. 505923), 60-year-old man. Multiple nodules with amorphous and reticular infiltrates bilaterally. Primary: osteogenic sarcoma right femur superimposed on Paget's disease of bone. Diagnosis primary: June 12, 1942. First evidence of pulmonary metastases: dyspnea, date of onset unknown. Death: Dec. 10, 1943.

TABLE III. PULMONARY METASTASES CLASSIFIED BY RADIOLOGIC APPEARANCE

NEOPLASM	NODULAR	AMORPHOUS	LYMPHANGITIC	MILIARY	MASSIVE CONSOLIDATION	MIXED
Carcinoma	140	12	16	10	2	17
Sarcoma	38	0	0	2	1	2
Melanoblastoma	13	1	0	0	1	0
Teratoma, testis	15	1	1	0	0	0
Hypernephroma	15	2	2	0	0	2
Endothelioma (Ewing's tumor)	8	0	0	0	0	0
Chorioepithelioma						
Testis	3	0	0	0	0	0
Uteri	4	0	0	0	0	0
Wilms's tumor	4	1	0	0	0	0
Sympathoblastoma	0	0	0	1	0	0
Malignant disease Unspecified	5	0	0	0	0	0
Totals	245	17	19	13	4	21

be classified under two or more headings. Such overlapping may be seen in the terminal stages of malignant disease when the lungs are inundated with increasing numbers of neoplastic cells, the hilar nodes are blocked, and extensive retrograde spread has occurred through lymphatic channels. In such a situation a lesion which has been plainly nodular for many months may exhibit a miliary admixture (see Fig. 8) with amorphous or reticular infiltrates.

In the 19 patients whose pulmonary lesions were classified as lymphangitic the primaries were located as follows: 16 carcinomas, 9 of breast, 3 of bronchus, and 1 each of esophagus, prostate, stomach, and tonsil; two hypernephromas; and 1 teratoma testis. Of the 13 in the miliary group there were 10 carcinomas, 3 of breast, 2 bronchus, and 1 each of thyroid and stomach; two sarcomas, 1 of liver and 1 of skin; and 1 sympathoblastoma of the adrenal.

A number of somewhat unrelated generalizations can be made from the data in Table IV: (1) more metastases occur in the right lung than in the left. This

TABLE IV. X-RAY APPEARANCE AND TIME RELATIONS OF PULMONARY METASTASES

NEOPLASM	NUMBER	AVERAGE NUMBER NODULES WHEN FIRST SEEN		AVERAGE DIAMETER NODULES (CM.)	NUMBER NODULES 5 CM. OR MORE IN DIAMETER	ONSET OF PRIMARY TO APPEARANCE OF PULMONARY METASTASES (MO.)	APPEARANCE PULMONARY METASTASES TO DEATH (MO.)
		RIGHT LUNG	LEFT LUNG				
Carcinoma							
Breast	71	2.6	1.9	1.2	1	32.2	8.2
Colon	22	4.1	2.5	1.6	0	29.1	6.1
Bronchus	14	1.1	1.1	1.3	0	14.8	2.8
Cervix	14	3.6	3.0	1.2	0	47.8	6.2
Thyroid	10	2.5	2.5	2.0	1	29.0	18.0
Total, average	130	3.0	2.1	1.4	2	32.0	7.5
Sarcoma	43	3.0	2.5	2.4	11	17.0	7.0
Hypernephroma	20	3.6	2.0	1.9	1	10.7	9.4
Melanoblastoma	15	6.6	3.6	2.1	2	32.5	4.1
Teratoma testis	14	5.7	5.2	2.2	2	10.3	3.2

may be due to the fact that the right lung is larger than the left and that its vessels compose a greater network in which tumor emboli are caught. (2) The nodular metastases which attain the largest size are those of sarcomas. (3) Teratomas of the testis have the shortest latent period (length of time between the first obvious manifestations of the primary and the radiologic evidence of pulmonary metastasis) of the five major groups which metastasize to lung. The period between the appearance of the pulmonary metastases and the death of the patient is also shorter in this group. Rather surprisingly, melanoblastomas, which are also rapidly fatal once established in the lungs, have the longest latent period.

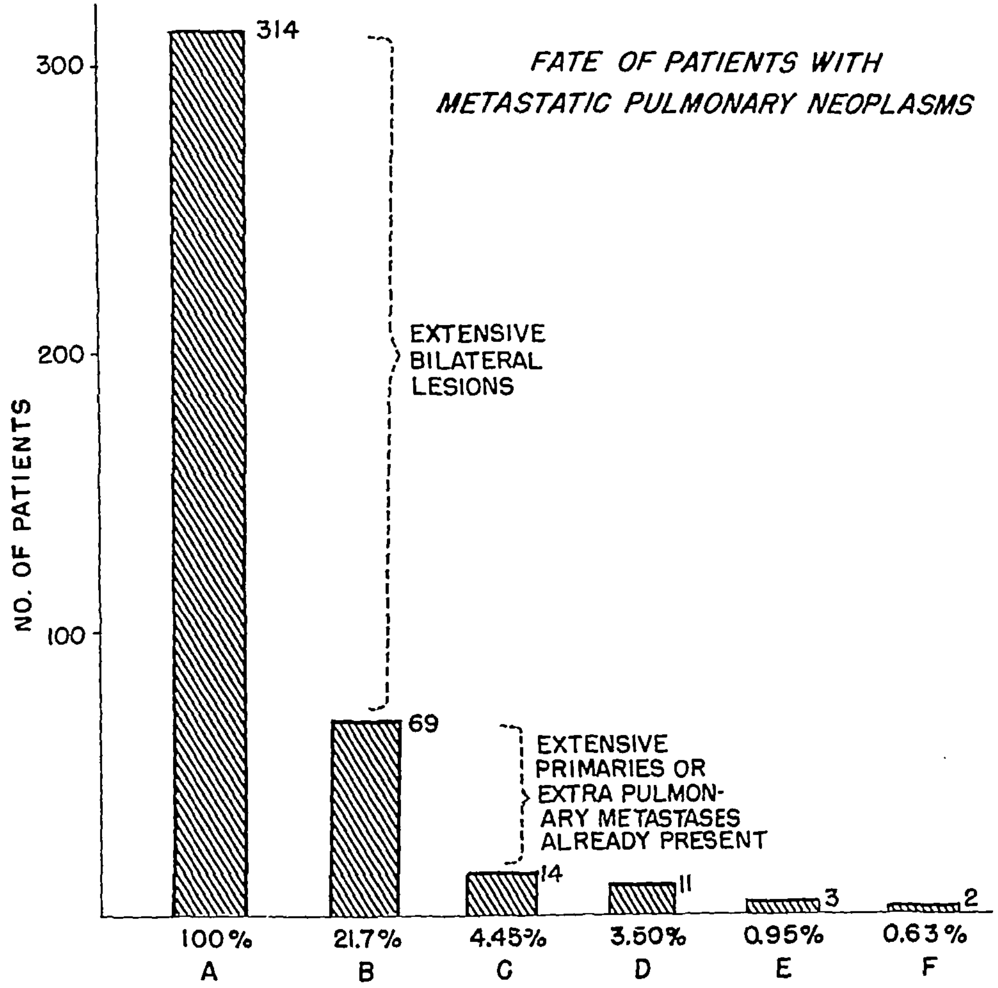

Fig. 9.—*A*, Total number of pulmonary metastases. *B*, Pulmonary resection anatomically feasible. *C*, Primary apparently controlled. *D*, Later development of extrapulmonary metastases or recurrence of primary. *E*, Fate unknown. *F*, Pulmonary resection carried out.

In 69, or 21.9 per cent, of the 314 metastatic pulmonary lesions resection appeared feasible from the standpoint of number and distribution in the lungs, in so far as these factors could be determined from roentgenograms. However, this is not the only consideration with regard to cure. In some of these 69 the primary growth had invaded vital structures or extensive recurrence had already followed removal. In other instances extrapulmonary metastases which were ineradicable were already present or *eventually* developed. There were only 4 patients, or 1.2 per cent of the original 314, in whom the primary was ultimately adequately controlled, extrapulmonary metastases were absent throughout the period of observation, and the pulmonary lesions were so situated that they could be completely removed. Two of these were operated upon by Dr. John Alexander and, at last examination, seven years and four years after resection of pulmonary tissue containing the lesions, were free of malignant disease, so far as could be determined.[1]* (See Fig. 9.)

Information about the incidence of recurrence of the primary and eventual development of extrapulmonary metastases is not without value. This information, however, is obtainable only by retrospection and is obviously not available in any instance at the moment of decision in dealing with malignant lesions.[2] Time is an important factor. That there will be local recurrences or distant metastases after pulmonary resection in a certain proportion of patients is obvious; but this risk of postoperative recurrence or further metastasis is not sufficient reason to withhold treatment which may result in a significant added number of cures. In short, in a patient whose primary lesion has apparently been successfully treated, who has one or more pulmonary metastases so located that they can be resected without removing more than the volume of one lung, and who has no discoverable extrapulmonary metastases, the pulmonary lesion should be resected without delay.

CONCLUSIONS

1. In a five-year period at the University of Michigan Hospital 314 patients were found who satisfied rigid clinical, pathologic, and radiologic criteria for pulmonary metastases from a malignant primary tumor.

2. Carcinoma of the breast was the commonest primary lesion, though not the highest in incidence of metastasis. It had the greatest degree of pleomorphism in the lungs; it also metastasized, in addition to lung, to mediastinum and pleura in a higher proportion than did any other primary malignant lesion in this series.

3. The distribution of symptoms was determined among the 172 patients who were noted to have symptoms. As a rule the presence or severity of symptoms was not related to the form or collective size of the pulmonary metastases.

4. Nodular metastases in lung may cavitate to produce a thick-walled defect not unlike an abscess.

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*Although reports of these patients have appeared in full elsewhere,[1] it might be pertinent to state a few facts about each. The first patient was a young woman who had had a spindle cell neurogenic sarcoma of the left forearm excised at another hospital. Re-exploration of the forearm a year later revealed only a benign neuroma in the stump of the ulnar nerve, but roentgenograms of the chest showed the presence of a solitary metastasis in the right lower lobe. This was immediately removed since there was no suspicion of local recurrence. A year later the left upper lobe, containing a mass which had been known to be present for the preceding five months, was removed. Both lesions were reported by the Department of Pathology at the University of Michigan Hospital as spindle-cell sarcoma metastatic to lung. Seven years after this second lobectomy the patient was well with no evidence of recurrence or metastasis.

The second patient was a middle-aged surgeon who developed a mass in the soft tissues of the right thigh anterolaterally. On removal this proved to be a spindle-cell fibrosarcoma. A recurrence in the scar was excised six months later and x-ray therapy given locally. One year after this the upper lobe of the right lung was removed because of the recent appearance in the roentgenogram of a small nodule. This was found to be spindle-cell sarcoma, like that from the thigh. Four years later there was no evidence of neoplastic disease.

5. Pulmonary metastases were classified by their radiologic appearance into five groups: nodular, amorphous (infiltrative), lymphangitic, miliary, and massive consolidation.

6. More metastases occurred in the right lung than in the left.

7. In this series, the pulmonary metastases of sarcoma attained a larger size than those of any other neoplasm.

8. Teratomas of the testis have the shortest "latent period" and the shortest "survival period."

9. Melanoblastomas have the longest latent period.

10. In only 21.9 per cent of the 314 cases was resection of the metastatic pulmonary lesion practicable from the standpoint of anatomic distribution as determined roentgenographically. Other considerations such as extent of invasion of vital structures by the primary and the presence of extrapulmonary metastases reduced the number on which operation could possibly have been considered to about 11.9 per cent.

11. Operation was actually carried out in only 0.63 per cent, or two patients. These two patients, however, are still alive and free of malignant disease more than four and seven years after their pulmonary resections.

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HIGH SEGMENTAL SPINAL ANESTHESIA

A Preliminary Report

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ONE of the most difficult problems confronting the surgeon and anesthetist for many years has been the selection and administration of an anesthetic to the patient undergoing surgery for pulmonary tuberculosis. The wide variety of anesthetic techniques suggested by various authors for the performance of thoracoplastics attests to the lack of suitability of any one method. Cervical intrathecal puncture, single dose, segmental spinal anesthesia comes close to solving the problem.

The advent of spinal anesthesia lessened the hazards and greatly aided the execution of abdominal surgery in phthisical patients. This technique continues to be the universal choice in the tuberculous patient undergoing abdominal operations. However, the vast majority of surgery in this disease involves the thorax, and here spinal anesthesia generally has been regarded as too dangerous, gaining only a few adherents. Honan,[1] in 1930, and Bettman and Biesenthal,[2] in 1931, were early enthusiasts for the use of spinal anesthesia in thoracoplasties. Later workers searching about for some satisfactory type of anesthesia for this work gave the intrathecal method a trial. Shields[3, 4] advocated spinal anesthesia for thoracoplasties with procaine hydrochloride inserted through a lumbar interspace with the patient placed in a marked Trendelenburg position. Gurd, Vineberg, and Bourne[5, 6] used the Etherington-Wilson technique[7] which depended upon a large dose of nupercaine to rise from the lumbar area of the spinal canal to the cervical region while the patient was in a sitting position. Willauer and associates,[8] in 1947, suggested the use of continuous spinal anesthesia with an intermittent dose of procaine hydrochloride delivered in a needle inserted in the lumbar area, and the patient in a fifteen degree Trendelenburg position. Many other surgeons tried spinal anesthesia for extrapleural thoracic procedures but abandoned it because, as Coryllos[9] stated, "a marked drop in blood pressure occurred frequently and could not always be controlled."

Any technique of inducing spinal anesthesia that necessitates the introduction of a large dose of anesthetic drug in a lumbar intervertebral space, which is then permitted to run upward throughout the length of the spinal canal to the cervical area, results in a generalized physiologic disturbance. The entire sympathetic chain is anesthetized, widespread vasodilatation occurs, and alarming circulatory collapse and intercostal paralysis follow. With a small dose of highly diluted anesthetic drug deposited in the spinal canal at the level

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throws the seventh cervical spinous process into prominence. The skin is prepared and after a skin wheal is made over the seventh cervical intervertebral space, a two-inch, 22 gauge short bevel needle, attached to a 2 c.c. syringe, is then inserted into the intrathecal space.

Constant suction should be maintained within the syringe so that the moment the bevel enters the intrathecal space spinal fluid will be aspirated, thus minimizing the danger of

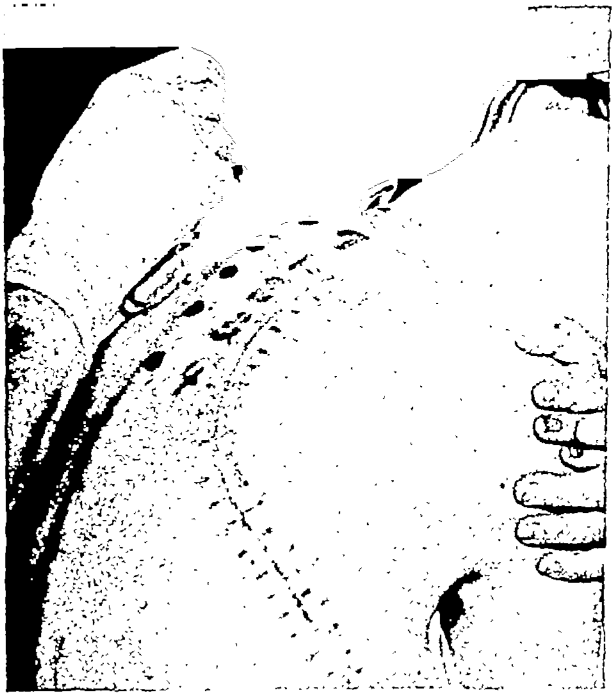

Fig. 2, *A*.—Photograph demonstrating the position of the patient and angle of the needle for intrathecal puncture. Care must be taken to maintain constant suction in the syringe.

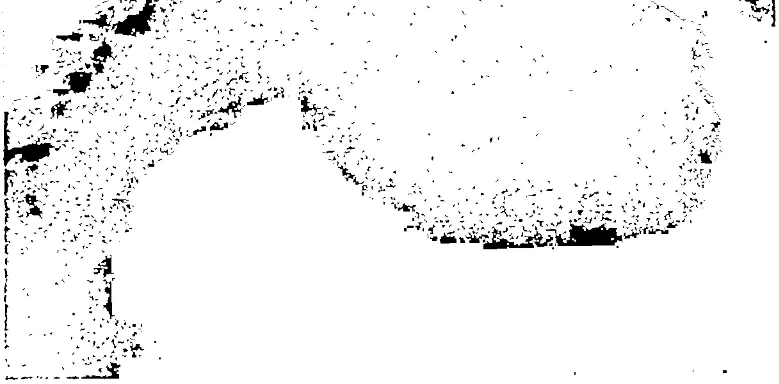

Fig. 2, *B*.—Roentgenogram demonstrating position of two-inch, 22 gauge needle in seventh cervical intervertebral space.

puncturing the cord. Enough cerebrospinal fluid is removed to make a 1 per cent solution when mixed with niphanoid pontocaine. Of this, usually 4 mg. are diluted with one and one-half times its volume of 10 per cent dextrose. Four-tenths cubic centimeter of 1 per cent neosynephrin is then added to this mixture. This solution is injected with the bevel of the spinal needle pointed caudad and at the approximate rate of ¼ c.c. per second. The patient is immediately placed in the lateral recumbent position with the operative side uppermost. The head is placed on a pillow so that the cervical cord is acutely elevated and the table is maintained at a horizontal level. A BLB mask is tightly fitted on the patient's face and oxygen is allowed to flow at ten liters per minute. The operative field is prepared and the surgical procedure is begun.

STUDY OF CASES

This study comprises a series of seventy-five thoracic operations done under spinal anesthesia (Table I). The operations were largely thoracoplastics, first, second, and third stages. The patients were an average group of tuberculous sanatorium cases of both sexes ranging in age from 18 to 63 years. Fifty-eight operations were done on patients classified as far advanced and fourteen operations on patients classified as moderately advanced. In six cases an extrapleural pneumothorax was done. The thoracoplastics were typical two or three stage, five- to seven-rib procedures performed through a posterior incision in all instances. The longest operation lasted two hours and twenty minutes and the shortest forty minutes. The average operating time was approximately one and one-half hours. Occasionally it is necessary to administer an intravenous narcotic to quiet an apprehensive or uncooperative patient. All patients received a supportive transfusion of 500 c.c. of whole blood given throughout the course of the operation.

There were no deaths in the group, neither immediate nor late. Central respiratory paralysis was not encountered, although an accident of this nature was feared and preparations made to combat it in every case. The respiratory minute volume was depressed on the average of about 30 per cent (see Table II). The fullest possible oxygenation was insured by the administration of oxygen at ten liters per minute by an efficient BLB mask. Spinal headache was encountered in one case and this was completely relieved with a few oral doses of nicotinic acid.

DISCUSSION

The advantages of this type of anesthesia in extrapleural thoracic operations, especially for thoracoplastics, appear multifold.

The administration is simple and rapid. The approach through the seventh cervical intervertebral space is by far the easiest entrance to the spinal canal.

The patients are free from pain and discomfort during the operation and muscular relaxation is adequate for the surgical procedure.

The vasomotor tone remains constant and little or no change was noted in the blood pressure of these patients after the anesthetic was given. There is no need for prespinal vasoconstrictor drugs. In about one-half of the cases in the series desoxyephedrine hydrochloride (Drinalfa) was given intramuscularly just prior to administering the spinal anesthetic to support the blood pressure.

TABLE II. SERIES OF TEN CONSECUTIVE

CASE	SEX	AGE (YR.)	DATE	CLASSIFICATION OF DISEASE	SITE OF SPINAL PUNCTURE	ANESTHETIC DRUGS AND DOSE	TYPE OF OPERATION
J. B. 4591	F	27	5/24/49	Moderately advanced	C_7	Pontocaine 6 mg., glucose 1 c.c., neosynephrin 0.4 c.c.	1st stage thoracoplasty
R. O. 4570	F	29	5/24/49	Far-advanced contralateral extrapleural oleothorax	C_7	Pontocaine 4 mg., glucose 0.6 c.c., neosynephrin 0.4 c.c.	Revision of thoracoplasty
G. M. 4560	M	53	5/26/49	Far-advanced contralateral lesion	C_7	Pontocaine 5 mg., glucose 0.7 c.c., neosynephrin 0.4 c.c.	1st stage thoracoplasty
E. L. 4443	F	32	5/26/49	Moderately advanced	C_7	Pontocaine 5 mg., glucose 0.7 c.c., neosynephrin 0.4 c.c.	2nd stage thoracoplasty
V. N. 4581	F	28	5/31/49	Far-advanced contralateral lesion	C_7	Pontocaine 4 mg., glucose 0.6 c.c., neosynephrin 0.4 c.c.	2nd stage thoracoplasty
R. R. 4570	M	43	5/31/49	Far-advanced contralateral lesion	C_7	Pontocaine 5 mg., glucose 0.7 c.c., neosynephrin 0.4 c.c.	1st stage thoracoplasty
B. V. 4613	F	47	6/ 2/49	Far-advanced	C_7	Pontocaine 4 mg., glucose 0.6 c.c., neosynephrin 0.4 c.c.	3rd stage thoracoplasty
S. K. 4203	M	63	6/ 2/49	Far-advanced	C_7	Pontocaine 4 mg., glucose 0.6 c.c., neosynephrin 0.4 c.c.	1st stage thoracoplasty
J. B. 4591	F	27	6/ 7/49	Moderately advanced	C_7	Pontocaine 4 mg., glucose 0.6 c.c., neosynephrin 0.4 c.c.	2nd stage thoracoplasty
G. M. 4560	M	53	6/ 7/49	Far-advanced contralateral lesion	C_7	Pontocaine 4 mg., glucose 0.6 c.c., neosynephrin 0.4 c.c.	2nd stage thoracoplasty

This was subsequently omitted from the routine preoperative management and in the latter one-half of the study the blood pressure of the patients remained relatively constant during the operation despite the lack of a vasoconstrictor drug.

The cough reflex is retained during the operation. Apparently the anesthetic dose is so small and diluted that the motor component of the intercostal nerves is only partially anesthetized, usually allowing a liberal degree of intercostal respiration. Furthermore, inasmuch as the anesthesia is segmental and the anesthetic level extends caudad only to the umbilicus, the action of coughing is still aided by the abdominal muscles. There is usually about a 50 per cent motor loss in the upper extremities but skin sensation of the arms and hands is consistently absent. There is no paresis, anesthesia, or paresthesia of the lower trunk or extremities. The patient frequently is able to move unassisted from the operating table to the litter when the surgery is completed.

Operations Giving Detailed Information

DURATION OF OPERATION	SUPPLEMENT TO ANESTHESIA	BLOOD PRESSURE DURING THE OPERATION		PREOP. VITAL CAPACITY (C.C.)	VITAL CAPACITY 5 MINUTES AFTER ADMINISTERING SPINAL (C.C.)	PER CENT REDUCTION IN VITAL CAPACITY	COMMENTS
		HIGH	LOW				
1 hr. 55 min.	Demerol 75 mg. I.V.	120/80	120/80	3,650	2,750	24.6 of own vital capacity	
2 hr. 10 min.	None	120/90	90/70	1,300	1,000	23.0	Moderate cyanosis throughout
1 hr. 45 min.	Demerol 75 mg. I.V.	110/72	100/70	3,550	2,100	40.8	Irrational from medication
1 hr. 25 min.	None	180/110	140/90	Readings not taken			In addition to pulmonary disease patient had malignant hypertension
50 min.	None	100/60	96/60	2,200	1,500	31.8	
2 hr.	None	90/68	90/68	2,400	1,950	18.7	
52 min.	Demerol 100 mg. I.V.	140/90	110/80	1,400	1,300	7.1	
1 hr. 40 min.	None	120/90	110/80	1,770	1,450	18.0	
1 hr. 30 min.	None	122/80	90/74	2,800	1,500	46.4	
1 hr. 25 min.	None	112/88	108/80	3,000	2,250	25.0	

The postoperative course resembled that of patients operated upon under local anesthesia. Routinely, they were made ambulatory on the first postoperative day. On the second postoperative day a full diet was generally taken and retained. Nausea and vomiting was an uncommon postoperative occurrence.

The patients themselves expressed satisfaction with the anesthesia and, in many cases, where apprehension existed prior to the first stage, this disappeared after their initial experience and they accepted the anesthesia with full confidence for their subsequent stages.

Some of the disadvantages inherent in any type of regional anesthesia used for thoracic operations are present with high segmental spinal anesthesia. Of these should be mentioned the following:

If inadvertently a hole is made in the pleura and paradoxical respirations ensue, a repair of the pleural tear, or a moist gauze pack placed over the tear with continuous suction within the pleural cavity, will usually suffice to ameliorate the situation. In the event that severe paradoxical respiration develops and the respiratory exchange is reduced, an intratracheal tube can be inserted quickly and without difficulty after an adequate intravenous injection of pentothal-*d*-tubocurarine solution, after which assisted respiration can be carried out. This exigency was encountered in one case in the seventy-five operations.

The loss of the sensation of breathing is frightening to some patients and for this reason reassurance and heavy premedication should be used. This combination gives a cooperative, quiet, frequently dozing patient who usually does not remember having been to surgery.

The intrathecal puncture at the seventh cervical intervertebral space should be done with extreme caution so as not to injure the spinal cord. A short bevel, two-inch needle is used to prevent too deep a puncture, and will just reach through the dura in the average adult.

SUMMARY AND CONCLUSIONS

A series of seventy-five thoracic operations for pulmonary tuberculosis has been presented in which a new technique of inducing spinal anesthesia is described. The anesthesia appears to fulfill a much needed place in the surgery of pulmonary tuberculosis inasmuch as it combines advantages of general and local anesthesia without possessing the undesirable features of each.

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TREATMENT OF ENDOBRONCHIAL TUBERCULOSIS WITH STREPTOMYCIN

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HISTORY OF ENDOBRONCHIAL TUBERCULOSIS

A HISTORICAL review of the medical literature on the subject of endobronchial and endotracheal tuberculosis dates the recognition of this entity with the development of the bronchoscope by Chevalier Jackson. Pioneer work in the description of the lesions was made by both Jackson and Eloesser,[5] the latter having written a pioneer article on stenotic lesions of the trachea and bronchi in 1934. Others, including Samson,[8] 1936, Barnwell, Littig, and Culp,[2] 1937, Warren, Hammond, and Tuttle,[9] 1938, Dolley and Jones,[4] 1940, Chamberlain and Gordon,[3] 1942, Brewer and Bogen,[1] 1947, and Judd,[6] 1948, have all contributed to the literature on the subject.

In June, 1941, Chamberlain and Gordon[3] reported at The American Association for Thoracic Surgery in Toronto that the only form of therapy directed toward the cure of endobronchial tuberculosis other than external drainage of an abscessed fistula or lobectomy or thoracoplasty in treatment of the underlying cause was application of silver nitrate locally. They described improvement but cautioned against using the word "cure" with this method.

With the advent of streptomycin therapy and the research program being carried out by the Streptomycin Committee of the Veterans Administration,[7] several studies have been completed and reported.

CLASSIFICATION

The peroral Endoscopy Section at Fitzsimons General Hospital uses the following classification for the differentiation of endobronchial tuberculosis:

1. Hyperplastic
2. Submucosal
3. Ulcerative
4. Fibrostenotic

1. The hyperplastic lesion is a patch of hyperemic hyperplastic dull velvet color mucosa raised from the normal pink mucosa.

2. The submucosal lesion is usually defined as a tubercle with a characteristic opalescent yellow-white coloration over its tip and a ringlike area surrounding this similar to the hyperplastic lesion, but usually not as granular.

3. The ulcerative lesion is a depressed, shallow, deep red ulcer with a dark red hyperemic area surrounding it. The ulcer varies in size, shape, and position.

4. The fibrostenotic lesion is an old healed lesion with cicatricial areas in the bronchial walls causing various stages of contraction and stenosis of the lumen.

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Table I. Total Dose of Treatment

LESION	TOTAL PATIENTS	DOSE IN GRAMS									
		UNDER 28	28	28 TO 41	42	43 TO 59	60 TO 90	91 TO 120	120 TO 155	156 TO 172	224
Hyperplastic	23	1	3	4	5	3	4	1	0	2	0
Submucosal	15	0	2	2	5	1	2	2	1	1	0
Ulcerative	11	0	2	1	2	1	0	2	2	0	1
Fibrostenotic	19	0	0	0	0	0	0	0	0	0	0

STATISTICS

From June 1, 1947, to February 28, 1949, 1,882 patients were examined bronchoscopically in the Peroral Endoscopy Clinic of Fitzsimons General Hospital, of whom 1,108 had a clinical diagnosis of pulmonary tuberculosis. Ninety-two patients or 8.3 per cent of the latter cases had evidence of endotracheal or endobronchial tuberculosis. Of these, 24 patients were lost to the study by transfer from the hospital and 49 were followed to healing after treatment with streptomycin. Twenty-three cases were diagnosed as hyperplastic type, 15 were of the submucosal type and 11 were of the ulcerative type. Nineteen patients with fibrostenotic endobronchial tuberculosis were also observed in this series but were not treated with streptomycin since no activity was present. One hundred twenty-nine bronchoscopic examinations were performed on the patients or an average of 3.1 examinations was performed on each patient.

Table II. Dose Plan of Treatment

LESION	TOTAL PATIENTS	DOSE IN GRAMS					
		DAILY		DAILY TWICE	THREE TIMES DAILY		DAILY
		0.5	1	1	1	2	2
Hyperplastic	23	1	15	1	3	3	0
Submucosal	15	0	14	0	1	0	0
Ulcerative	11	0	8	0	1	1	1
Fibrostenotic	19	0	0	0	0	0	0

In this study, 15 of the 23 cases of hyperplastic endobronchial tuberculosis were treated with 1 Gm. streptomycin intramuscularly daily, and the others in this group included varying dosages (see Table II). Fourteen of the 15 patients with submucosal endobronchial tuberculosis were treated with 1 Gm. streptomycin intramusculary daily, and 8 of the 11 patients with ulcerative endobronchial tuberculosis were treated with 1 Gm. streptomycin intramuscularly daily. The earliest healing seen in the hyperplastic type was twenty-eight days and the longest healing seen was over 120 days with a mean healing of forty-two days. Similar figures prevail for healing in the submucosal type with a mean healing time of slightly over forty-two days. Six patients with ulcerative endobronchial tuberculosis were healed in over forty-two days and 5 patients were healed in less than forty-two days (see Tables I and III).

Table III. Complications on Healing

Hyperplastic	None in 23 cases
Submucosal	None in 15 cases
Ulcerative	3 cases of 11 healed with stenosis

DISCUSSION

The Report to the Council of The American Medical Association[7] based on data submitted to the Fifth Streptomycin Conference in Chicago during April, 1948, summarized the result of streptomycin therapy in 112 cases of tracheobronchial tuberculosis. The evidence of tuberculous causation in the presence of repeatedly positive bronchoscopic observations was accepted in this study as in the Report to the Council by the demonstration of acid-fast bacilli in the sputum by culture. No patients in this study group were treated by streptomycin aerosol inhalation as this procedure was abandoned by previous investigators in favor of the intramuscular route.

The Report to the Council of The American Medical Association in October, 1948, noted that between 80 and 90 per cent of the lesions were reported as either healed or improved. These results were less constant than those of Brewer and Bogen who, in 1947, reported 100 per cent healing with 2 Gm. streptomycin intramuscularly daily in 13 patients with ulcerative lesions. The explanation offered for this difference was the tendency to include inflammatory lesions as distinct from the purely ulcerative lesions analyzed by Brewer and Bogen.

In the series studied in the paper, complete healing without residual fibrosis occurred in 100 per cent of the 23 patients with hyperplastic endobronchial tuberculosis and complete healing without residual fibrosis was noted in 100 per cent of the 15 patients with submucosal endobronchial tuberculosis. Three patients in the group of 11 with the diagnosis of ulcerative endobronchial tuberculosis healed with residual stenosis. Ten per cent of the cases included in the Fifth Conference figure were of the fibrostenotic type. Twenty-two per cent of the cases diagnosed as endobronchial tuberculosis in this series were of the fibrostenotic type of endobronchial tuberculosis.

It is of interest to note that complete healing occurred without residual fibrosis in the hyperplastic and submucosal types of diseases and that the residual fibrosis which was observed occurred only in cases of ulcerative endobronchial tuberculosis. This fact has considerable clinical significance when it is remembered that all that could be hoped for prior to streptomycin therapy was that the disease would run its "natural" course and heal with a minimal amount of stenosis and mechanical obstruction and that no further extension or spread would occur secondarily.

SUMMARY

1. A group of 49 patients with active endobronchial tuberculosis treated with streptomycin and followed to healing are reported.

2. The majority of the patients received 1 Gm. streptomycin intramuscularly daily.

3. The average healing time for hyperplastic endobronchial tuberculosis was 42 days, for submucosal endobronchial tuberculosis 42 days, and slightly longer for ulcerative endobronchial tuberculosis.

4. All patients healed without residual fibrosis except 3 patients with ulcerative endobronchial tuberculosis and these healed with some degree of stenosis.

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CANCER OF THE CERVICAL ESOPHAGUS

With a Case Report

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SINCE 1938, tremendous strides have been made in the surgical management of malignant diseases of the esophagus, more notably in the regions of the middle and lower thirds of the esophagus. Management of a malignant lesion in the upper or cervical esophagus still presents a problem. While the surgical approach in the middle and lower thirds has become rather standardized, a lesion in the upper third is handled in a variety of ways by different surgeons. This, together with the infrequent reports of lesions in this area treated by surgery, as contrasted with the numerous reports on lesions in the middle and lower thirds, signifies, as yet, lack of agreement on a completely satisfactory procedure.

Carcinoma of the esophagus is generally considered to comprise 5 per cent of all malignant diseases. In the United States, Hoffman[1] found the mortality from carcinoma of the esophagus exceeds 200 per year. In 8,572 collected cases, Ochsner and DeBakey[2] found 1,717 cases (20 per cent) were located in the upper third of the esophagus. Thus, it behooves the surgeon to strive for a satisfactory approach to the management of lesions in this area.

HISTORY

In 1871, Billroth[3] demonstrated that resection of the cervical esophagus was feasible in dogs. Czerny,[4] in 1877, reported the first successful removal of carcinoma in the cervical esophagus in man; the patient lived fifteen months and died of a recurrence. In 1884, Von Mikulicz[5] reported the successful removal of the cervical esophagus, and the subsequent plastic repair of the defect by a skin-lined tube.

Esophagogastrostomy was first done on dogs in 1895, by Biondi.[6] Among the first to propose esophagogastrostomy after esophagectomy in man was Gosset[7] in 1903. In his reports on the procedure in dogs, he first called attention to the importance of anchor sutures to relieve tension on the anastomosis. The first successful case of esophagectomy for carcinoma of the lower esophagus, and esophagogastrostomy over a Murphy button (Wendel's technique), was presented by Adams and Phemister,[8] in 1938.

Garlock,[9] in 1943, started to mobilize the stomach for esophagogastrostomy high in the thorax and found he was able to deliver the stomach up to the apex of the thorax without endangering the blood supply or causing tension on the anastomotic suture line.

Several reports are now present in the literature concerning radical esophagectomy with cervical esophagogastrostomy. The first reported successful

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case was by Sweet[10] in 1948. This was followed by reports from O'Donnell,[11] Wylie and Frazell,[12] Brewer,[13] and Nissen.[14] The two cases of O'Donnell and Brewer are the only known reports of carcinoma of the cervical esophagus treated in this manner to date.

PRESENT TECHNIQUES

Today there are two principal procedures practiced in surgery for carcinoma of the upper esophagus. One is a local block resection with subsequent repair by a skin-lined tube, most popularly fashioned after the method of Wookey.[15] The other involves almost a total esophagectomy with removal of all major lymph channels draining the area, through a transthoracic approach, and transphrenic mobilization of the stomach for a cervical esophagogastrostomy to maintain continuity of the gastrointestinal tract.

In Wookey's two-stage method, the first stage consists of resection of the cervical segment and turning in of a rectangular flap of skin, subcutaneous fat, and platysma muscle. The flap is sutured to the hypopharynx above and to the distal esophagus below, leaving a temporary groove. At the second stage, several weeks later, this groove is closed to restore the continuity of the esophagus. Since, as a rule, the surgeon has access to only about four inches of the length of the esophagus, this procedure cannot include wide regional dissection. This, likewise, makes impossible the removal of the lymph nodes draining the area.

In the other approach, where suspicion exists of extension to the carotid sheath or the superior mediastinal structures, a low cervical incision may be made first to determine operability. The thorax is opened by a left posterolateral incision. The mediastinum is then opened above the arch of the aorta and the esophagus at this level is mobilized up to the cervical level. The remainder of the esophagus is freed from the mediastinum, the diaphragm opened widely, and the stomach and duodenum mobilized. The esophagus is divided at the cardia and the cardia is closed. The medial end of the left clavicle and anterior part of the first rib are then resected and the fully mobilized stomach passed through the thorax into the neck for a cervical esophagogastrostomy, consisting of a two-layer anastomosis of interrupted sutures. A small Penrose drain is left in the cervical wound and an intercostal catheter within the pleural space for suction drainage.

COMMENTS

While the symptoms of carcinoma of the esophagus, such as dysphagia, pain, loss of weight, vomiting, hoarseness, bleeding, and coughing, are classical when present, they often bespeak a late or extensive lesion. This is especially true in carcinoma of the upper esophagus. Moreover, carcinoma of the esophagus, even when far from the cardia, metastasizes to regional lymph nodes at the level of the tumor and below the tumor as demonstrated by Sweet[16] and Gauthier-Villars and Dontzoff.[17] Thus, it is evident that the local resection of a cervical esophageal carcinoma will be adequate only in the rare case of an early, small, low-grade malignant lesion, and the surgeon will always be in doubt as to the status of the lymph nodes in the superior mediastinum, hilar region, periesophageal, pericardial, and left gastric regions. Also, from the standpoint of the patient, a plastic repair with a skin-lined tube is seldom completely satisfactory, due to frequent failures in ideal anastomosis between skin and esophageal tissue. The radical procedure would seem more ideally to answer the requirements of adequate cancer therapy, namely, a wide block resection of the lesion and adjacent tissue and removal of all lymph nodes in the areas of frequent metastasis.

The aim of cancer surgery is to cure the disease and thereby render the patient's life useful and enjoyable. The less radical approach has the advantage of a lower postoperative mortality and morbidity rate. However, since only an occasional early case can expect to be cured by this approach, the more radical resection should extend the number of cures.

Irradiation therapy has its proponents and especially is this true in the cervical area. There are several scattered reports of six-, seven-, and eight-year cures of carcinoma in this area using roentgen-ray therapy. However, irradiation therapy is of no value in cases of extension to the lymph nodes; therefore, the surgical removal of the lesion should afford a better chance for cure. It is doubtful if roentgen therapy should be used even in palliation unless the act of swallowing can be maintained and should be reserved for the early cases in which surgery is contraindicated, either due to extreme age or associated pathology. If the lesion is inoperable and complete obstruction has occurred, the only palliation to be offered is gastrostomy; however, this is strictly temporary—the prolonging of life being usually only three to six months with the patient usually unhappy due to symptoms and the loss of swallowing.

As pointed out by Lewis,[18] while carcinoma of the esophagus appears to be of low-grade malignancy, as viewed by the pathologist, the lesion is in the main of rather high malignancy, considering the length of time it takes to kill the patient and the liability to recur after an apparently adequate resection. Earlier recognition and still further improvements in technique are needed to extend the number of cures. Any symptoms referable to the esophagus should be investigated and the presence of dysphagia in a patient past the age of 40 years should not be dismissed until x-ray examinations with barium swallow and contrast media examination of the mucosa, esophagoscopy, and even bronchoscopy have been carried out. If a suspicious lesion is found, even if biopsy by esophagoscopy is negative, an exploration with adequate biopsy and examination of the lesion should not be deferred. Once a malignancy is found, when operable, as radical resection as possible should be carried out to fulfill the requirements of adequate cancer therapy.

CASE REPORT

The following case of carcinoma of the upper esophagus with a successful radical resection and cervical esophagogastrostomy is presented.

J. M., a 64-year-old white man, entered Mt. Carmel Hospital on Jan. 4, 1949. Complaint was dysphagia of three months' duration, gradually progressing to the point where only liquids could be swallowed. There was a weight loss of twenty-eight pounds.

Physical examination was essentially negative.

During the procedure the patient received 2,000 c.c. of whole blood. Bronchoscopy was done before leaving the operating room. The postoperative blood pressure was 100 systolic and 70 diastolic.

The surgical specimen (Fig. 2) consisted of 19 cm. of esophagus. On opening the esophagus, a large ulcerated mass with a necrotic center was found involving the upper segment. With the exception of about .5 cm., the tumor completely encircled the esophagus. The tumor appeared to involve the wall, and the wall of the esophagus in this area was considerably thickened. A close examination of the tissue revealed no involved lymph nodes. Microscopic examination revealed squamous-cell carcinoma, grade 3 malignancy, with some invasion of the muscularis but no evidence of extension through the muscularis. The mucosa at the proximal end was free of tumor.*

Postoperatively the patient was placed on suction drainage of the chest. Penicillin and streptomycin were continued. Progres was satisfactory and the drainage tubes were removed the second postoperative day. The patient received 1,000 c.c. of blood after surgery. Early ambulation was employed. Food by mouth was given on the third day gradually increasing to a regular diet by the seventh day.

X-ray examination with barium (Fig. 3) revealed no evidence of obstruction at the anastomosis. The patient was discharged Jan. 29, 1949.

Follow-up examinations reveal the patient progressing satisfactorily. The only complaints are some slight discomforts and gas but he is swallowing well. At the last examination, June 18, 1949, the patient was doing well with no evidence of recurrence.

SUMMARY

A brief review of the literature is presented accompanied by a case report of removal of the upper portion of the esophagus including a portion of the cervical esophagus. An insufficient number of these cases have been done, apparently, to establish a definite criterion of technique. There, undoubtedly, have been other cases operated in somewhat this manner but they have not been reported in the literature at this time. No attempt has been made to champion one technique or the other.

I have used the left-sided approach in all cases of esophageal resection so have had no experience with the right-sided approach. It is my feeling that the technique presented in this article is more feasible from many angles. The first thing is, it is done in one procedure; second, ample room is given at the site of anastomosis; third, it seems the anatomy is better adapted to the left approach.

It is somewhat questionable in my mind, whether it is necessary to remove the clavicle and first rib, as it seems quite probable there is sufficient space to bring the stomach posterior to the subclavian vessels instead of anterior. However, at the time I performed this operation, I felt that this might possibly produce mechanical obstruction from surrounding structures.

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THE DIFFERENTIAL DIAGNOSIS OF UNRESOLVED PNEUMONIA AND BRONCHIOGENIC CARCINOMA BY PULMONARY ANGIOGRAPHY

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INTRODUCTION

UNRESOLVED pneumonia may simulate bronchial carcinoma clinically and roentgenographically. Differentiation of these conditions may be difficult or impossible by the diagnostic aids now commonly used. Delayed resolution of a pulmonary parenchymal lesion should suggest a pathologic process of more serious nature than that of simple pneumonia. Physical findings, clinical course, temperature, leucocyte and sedimentation curves, and immediate response to therapy may be very similar in carcinoma and pneumonia. Bronchography, bronchoscopy, and cytologic studies are of great diagnostic value but are at times inconclusive in the diagnosis of bronchial carcinoma. The difference in the nature of the pathologic process and the difficulty in diagnosis by the usual means prompted us to study the vascular pattern of the lungs in search of a diagnostic adjuvant. Pulmonary angiography affords a means for conducting such a study in the living patient.

Since the original work on contrast visualization by Forssmann[1] and Moniz[2] and the detailed studies of pulmonary arteriography by Robb and Steinberg,[3, 4] little has been written about angiocardiography in pathologic states of the pulmonary parenchyma. Most discussions deal with the differentiation of mediastinal tumors, and some investigators[3, 4, 5] have described recognizable defects in the pulmonary trunks in bronchial carcinoma. We[6] have previously reported decreased vascularity of lung parenchyma within and distal to primary carcinoma. We are not aware of any report which deals with the changes in the vascular pattern in pneumonia.

CLINICAL MATERIAL

The study group comprised twenty-six patients with primary bronchial carcinoma and thirty-five patients with resolving or unresolved pneumonia. The diagnosis was established histologically in the cases of carcinoma and clinically in the pneumonia (that is, ultimate complete resolution of the inflammatory process and restoration of the individuals' previous state of health).

TECHNIQUE

For pulmonary arteriography the patient is seated before a radiographic screen which holds 14 by 17 inch cassettes. A specially constructed leaded tunnel device, manually operated, is used to permit exposures every two seconds, ordinarily for a total of four exposures. Fifty c.c. of 70 per cent Diodrast are injected into an antecubital vein through a No. 13 needle in an average

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From the Veterans Administration Hospital, Department of Internal Medicine.

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time of one and one-half seconds. The injection is done percutaneously. Timing is started when 35 to 40 c.c. have been injected. All films are taken at six feet, and the exposure factor is an additional 10 kv. over that for the ordinary six-foot film.

The right heart and pulmonary arterial tree are well outlined on the two-second film. Pulmonary veins and left atrium are visualized on the four- and six-second films. The left ventricle and outflow tract are outlined on the eight-second film.

FINDINGS

The pulmonary arterial pattern of normal lungs is ordinarily quite comparable on the two sides and there is a relative constancy of distribution throughout both lung fields (Fig. 1). The size and number of the arteries, when comparing the two lungs of the same individual, are much the same in the inner, middle, and outer lung zones (that is, secondary, tertiary, and smaller radicles), though the image is far from identical. The left pulmonary artery ordinarily courses higher than the right and curves quickly downward and backward, whereas the right trunk runs horizontally and varies considerably in length before dividing into upper and lower branches.

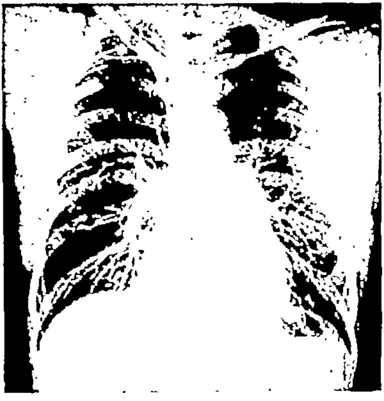

Fig. 1.—Normal pulmonary arteriogram showing the excellent contrast on the two-second film following the injection of 50 c.c. of Diodrast into an antecubital vein. The size, number, and distribution of the arterial radicles are quite comparable on the two sides.

Decreased vascularity of the pulmonary parenchyma was found in twenty-four of our twenty-six cases (92 per cent) of bronchial carcinoma (Figs. 2 and 3). Of the two cases in which this finding was not apparent, one had diffuse lymphangitic spread of neoplasm throughout the entire lung, and the other had extensive tracheal and bilateral bronchial involvement without extrinsic evidence of neoplasm.

In resolving and unresolved pneumonia there is a relative increase in the vascularity of the involved portion of lung when compared with uninvolved segments. In the late stages of resolution and after resolution is complete this

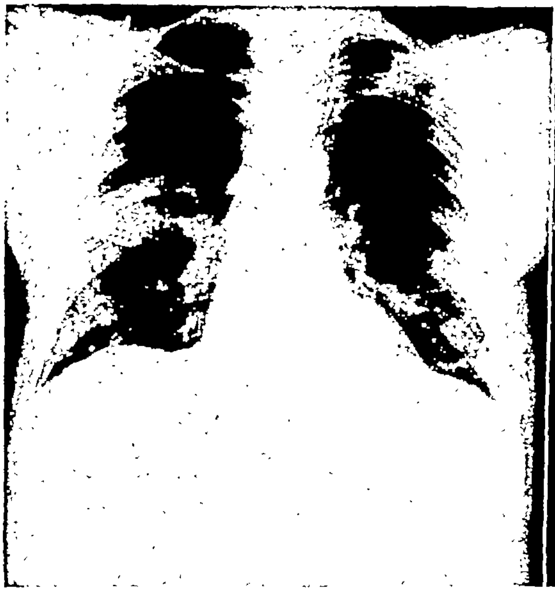

Fig. 2.

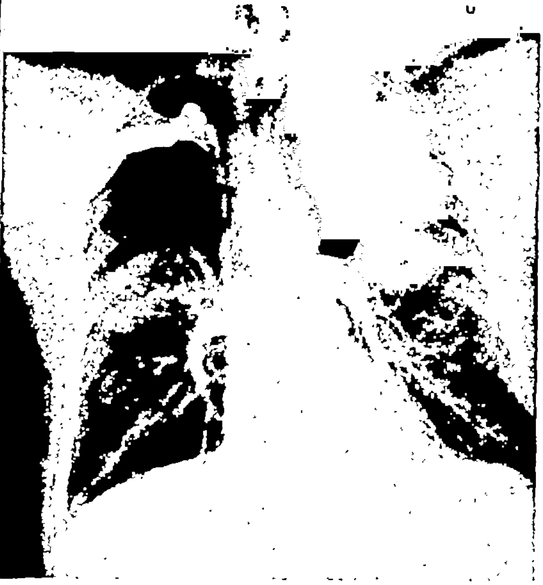

Fig. 3.

Figs. 2 and 3.—This patient, a 50-year-old white man, complained of chronic cough for many years and frequent upper respiratory infections for weeks prior to admission. The cough changed and became more productive and there was associated blood streaking. He had a low-grade fever, slight anemia, leucocytosis, and increased sedimentation rate. The arteriogram was done seven days after admission. Bronchoscopic diagnosis was asthmatic tracheobronchitis. Bronchial washings were positive for carcinoma. Pneumonectomy was done subsequently, and the final diagnosis was carcinoma, epidermoid, moderately well differentiated, right upper lobe bronchus.

Fig. 2, Bronchial carcinoma, plain film, interpreted originally as revolving pneumonia.

Fig. 3, Arteriogram, same patient as Fig. 2, showing decreased vascularity of the entire right upper lobe.

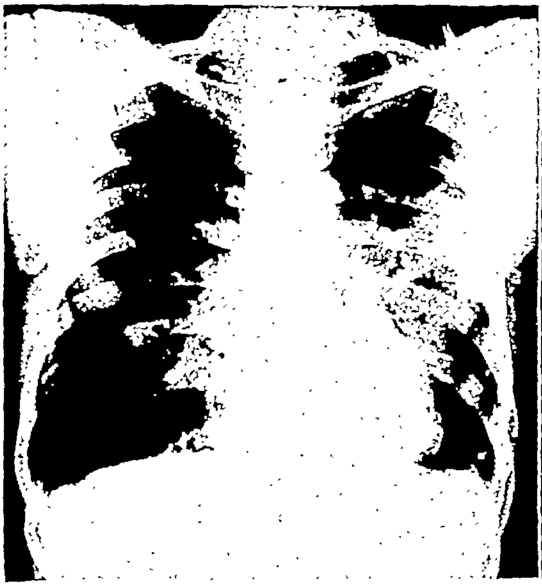

Fig. 4.

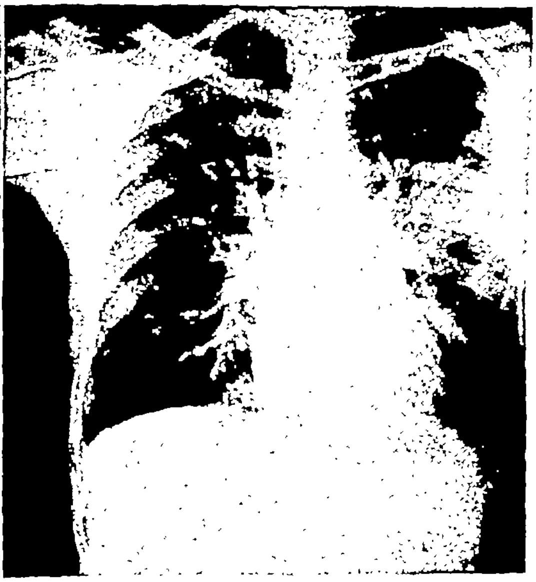

Fig. 5.

Figs. 4 and 5.—This 51-year-old white man entered the hospital complaining of left chest pain, fever, weight loss, and anorexia and gave the history of repeated episodes of pleurisy and pneumonia involving the left lung. He had a productive cough, low-grade fever, moderate leucocytosis, and an elevated sedimentation rate. Pulmonary arteriography was done seven days after admission. The lesion subsided completely after several weeks' hospitalization.

Fig. 4, Plain film, unresolved pneumonia, left mid-lung field.

Fig. 5, Arteriogram showing relative increase in vascularity of the left mid-lung field.

relative increase in vascularity is no longer present. The increase involves the secondary and lesser arterial radicles both in regard to size and number. (Figs. 4 and 5.) Twenty-six of the thirty-five cases showed relative increase in the vascularity of the segment of pneumonic lung as compared with the opposite lung. The remainder showed normal vascularity. (Most of these were done during the final stage of resolution.)

No case of pneumonia has shown decreased vascularity of the involved portion of lung.

DISCUSSION

The explanation of the vascular changes found is based on the fundamental differences of the pathologic processes. Numerous textbooks of pathology mention increased vascularity evident to the naked eye in specimens of lung showing resolving pneumonia. The hyperemia involves predominantly the smaller vessels, and compensatory dilatation is present in the larger vessels supplying the inflamed portion of lung. Anderson[7] described the process of resolution: "When most of the exudate has been absorbed but before re-expansion has occurred, the appearance is simply that of atelectasis and hyperemia with more or less edema." The presence of atelectasis within the area, by increasing the density to the roentgen ray, may serve to accentuate the presence of relative increase in vascularity on the angiogram. Karsner[8] stated that after complete resolution, hyperemia lasts for "over a few weeks."

The factors which produce the picture of decreased vascularity within and distal to carcinoma, in our opinion, are: (1) compression and obstruction of arterial radicles by expanding and infiltrating neoplasm; (2) compensatory emphysema due to partial bronchial obstruction; (3) necrosis of lung tissue.[6]

SUMMARY

We have found pulmonary arteriography useful in the differentiation of unresolved pneumonia and bronchial carcinoma.

Increased or normal vascularity of the involved segment of lung is a characteristic finding in unresolved pneumonia, while decreased vascularity within and distal to the carcinoma is a very frequent finding (92 per cent of our series).

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EXCISIONAL SURGERY IN PULMONARY COCCIDIOIDOMYCOSIS

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INTRODUCTION

THE following is a report representing an attempt to tabulate the known cases of pulmonary coccidioidomycosis treated by excisional surgery.

Inquiries were sent out to all members of The American Association for Thoracic Surgery, as well as other individuals who might have occasion to carry out excisional surgery in this disease. Replies were received from 224 individuals. Geographically this represented 37 states in the United States, 9 different localities in Canada, as well as single replies from Hawaii and Sweden. There were 8 surgeons in California who reported, 4 surgeons in New York, 3 surgeons in Massachusetts, 3 surgeons in Arizona, and 2 surgeons in each of the following states: Missouri, Louisiana, North Carolina, Washington, D. C., Texas, and Wisconsin. In each of the following localities 1 surgeon reported: West Virginia, Minnesota, Utah, Colorado, Virginia, Tennessee, and Hawaii.

TABULATION OF INDIVIDUAL REPORTS

Greer, Forsee, Grow, and Mahon reported 9 lobectomies, and local excision in 4 others. The indications were persistent cavitation, recurrent hemorrhage, exclusion of neoplastic disease, and spontaneous pneumothorax, with failure of the lung to re-expand.

B. Cotton reported 5 pneumonectomies, 5 lobectomies, and 3 segmental resections. The indications were cavitation. There were no complications.

W. L. Rogers reported 8 cases. In 3, lobectomy was performed, and in the other 5 cases either a combination of enucleation of cavity or local excision was carried out. The indications were not stated. The complications were not stated.

D. W. Melick reported 1 pneumonectomy, 3 lobectomies, 2 enucleations, and in 2, local excision. The indications were persistent cavitation, recurrent hemorrhage, suspicion of neoplasm, and persistent bronchopleural fistula following spontaneous pneumothorax. Following lobectomy one patient developed a bronchopleural fistula, complicated by empyema. It was necessary to perform a thoracotomy, followed by thoracoplasty in order to effect a cure.

J. C. Jones reported 5 lobectomies. The indications were persistent cavitation, hemoptysis, and tension cavity. An empyema followed 1 lobectomy performed by the tourniquet technique. The empyema eventually cleared, and the patient is well at this time.

R. R. Shaw reported 1 lobectomy and 3 segmental resections. The indications were persistent cavitation and granuloma. Dr. Shaw described his cases of cavitation as often representing residual cyst due to epithelization of previous coccidioidal cavity. There were no complications.

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F. B. Berry reported 4 lobectomis. He failed to give his indications for surgery. Following lobectomy he reports a spread of the disease which was controlled by thoracoplasty.

O. T. Claggett reported 1 pneumonectomy, 1 lobectomy, and 1 local excision. The indications were pulmonary lesions of indeterminate etiology which had not responded to conservative measures. There were no complications.

T. B. Wiper reported 2 lobectomies and 1 segmental resection. The indication was cavitation. There were no complications.

T. H. Burford and E. A. Graham reported 2 lobectomies. The indication was cavitation. A complication in 1 case was empyema.

F. P. Coleman reported 2 lobectomies. The indication was cavitation. There were no complications.

G. V. Brindley, Jr., reported 2 lobectomies. The indications were not stated. There were no complications.

J. D. Murphy reported 2 lobectomies. The indication was cavitation. A complication in one was recavitation in the lower lobe on the side of upper lobectomy. A thoracoplasty failed to close the cavity. An Eloesser cavernostomy was performed, and smears from the cavity revealed acid-fast bacilli as well as coccidioidal spherules.

W. Weisel reported 2 lobectomies. The indication was hemoptysis. There *were no complications.*

J. Weinberg reported 1 pneumonectomy and 1 lobectomy. The indications were bronchopleural fistula and empyema in 1 case, and cavitation in the second case. At the time he performed the pneumonectomy, a pleural decortication was included.

H. Randolph reported 1 lobectomy and 1 pneumonectomy. The indications were cavitation and suspicion of carcinoma. There were no complications in the cavity case. The second patient died in the immediate postoperative period.

Max Chamberlain reported 1 lobectomy. The indication was suspicion of neoplasm. There were no complications.

J. B. Amberson reported 1 lobectomy. The indication was cavitation. There were no complications.

D. J. Dugan and P. C. Samson reported 1 lobectomy. The indications were cavitation and hemorrhage. There were no complications.

Krapin and Lovelock reported 1 lobectomy. The indications were cavitation and recurrent hemorrhage. A complication was recurrence of cavity in the lower lobe, eventually closed by thoracoplasty.

A. Ochsner reported 1 lobectomy. The indication was cavitation. There were no complications.

F. Raine reported 1 local excision. The indication was cavitation. There were no complications.

D. E. Harken reported 1 case. He does not state his indication or complications. He does state that a decortication for hemothorax was included simultaneously with the local excision of the coccidioidal lesion.

R. H. Sweet reported 1 lobectomy. The indication was cavitation. There were no complications.

R. A. Daniels, Jr., reported 1 lobectomy. The indications were cavitation, productive cough, and hemoptysis. There were no complications.

W. R. Rumel reported 1 lobectomy. The indication was cavitation. There were no complications.

Brian Blades reported 1 lobectomy. The indications were cavitation and hemoptysis. There were no complications.

L. Miscall reported 1 lobectomy. The indication was cavitation. There were no immediate complications, but two months following surgery, new cavities were present in the upper lobe on the opposite side to resection, and also cavitation in the lower lobe on the side of resection.

P. Sanger reported 1 segmental resection. The indication was cavitation. There were no complications.

H. E. Johnson reported 1 lobectomy. The indication was cavitation. There were no complications.

J. P. Lynch reported 1 lobectomy. The indications were cavitation and hemoptysis. There were no complications.

R. Ross reported 1 lobectomy. The indication was a round, solid lesion suspicious for carcinoma. There were no complications.

W. White, Jr., reported 1 segmental resection. He stated the diagnosis was not certain, however, although the microscopic appearance was consistent with a diagnosis of coccidioidomycosis.

J. W. Stacey reported 1 local excision. The indication was a round, solid lesion suspicious of carcinoma. There were no complications.

F. X. Byron reported 1 lobectomy. The indications were cavitation and hemorrhage. There were no complications.

E. D. Churchill reported 1 lobectomy. The indication was consolidation of the left upper lobe. There were no immediate postoperative complications but the patient died some weeks later of the disease. This lobectomy was carried out by the tourniquet method because of hilar adenopathy and inability to do an adequate individual ligation.

P. W. Gebauer reported 1 lobectomy. The indications were cavity and hemoptysis. There were no complications.

E. W. Davis reported 1 segmental resection. The indication was a solitary nodule suspicioned to be neoplastic. There were no complications.

E. Holman reported 1 lobectomy. The indication was cavitation. A complication was a bronchopleural fistula which followed the lobectomy. This resulted in empyema and necessitated a thoracoplasy from which the patient recovered and is now considered cured.

DISCUSSION

In addition to the excisional surgery, decortications were reported for coccidioidomycotic empyema or spontaneous pneumothorax resulting in failure of the lung to re-expand. Holman reported 1, Greer, Forsee, Grow, and Mahon reported 4, Harken reported 1, Weinberg reported 1, Cotton reported 2, and Melick reported one.

In at least 6 instances the surgeons reporting from the Eastern and Northern states recorded the fact that the patient contracted the fungus disease in the Southwest. No particular attempt was made to determine the mortality rate. There were, however, 3 deaths reported, 1 by Randolph, 1 by Harper, and 1 by Churchill.

COMMENTS OF DIFFERENT INDIVIDUALS IN REGARD TO SURGICAL THERAPY

Dr. David T. Smith of Duke University stated as follows: "It is my impression from seeing material at the Fitzsimmons Hospital in Denver that the minimum amount of surgery which removes a cavity is adequate. In some cases this has been segmental resection, but in most instances it has been lobectomy. Pneumonectomy only is needed if the disease is extensive and extended over two or more lobes."

F. J. Phillips had this to say: "From what I know of this disease I believe I would not hesitate to do a resection if there were an isolated lesion that had run a protracted course and there were no other contraindications."

Dr. Felix Hughes, Memphis, Tenn., said: "As far as coccidioidomycosis is concerned, it seems to me I recall that excisional surgery is not tolerated well."

Dr. David Creighton of New Rochelle, N. Y., said: "The problem of surgical procedure in coccidioidal cavitation is still a moot one. Its solution depends on an adequate follow-up study of present methods. Until such a study is available it is my feeling that excisional surgery, that is to say lobectomy, suffices. When more than one lobe is removed, however, adjunctive thoracoplasty will prevent the possible reactivation of invisible granulomatous foci by undue stretching of the remaining lung tissue. However, the use of thoracoplasty, previously a very tenable procedure, would be open to censure, in view of the recent mention of Dr. Smith in regards to cavity epithelization in coccidioidomycosis."

Dr. C. E. Smith of San Francisco, the Stanford University School of Medicine, stated: "As for the recurrence of cavities after thoracotomy and resection, in view of the apparent remoteness of that complication, it will require time to decide whether or not thoracoplasty should be performed soon after resection. One wonders if thoracoplasty might be reserved for the complication rather than carry it out as a prophylaxis against such a complication. My own position is that I do not believe in any intervention unless there are symptoms, and specific reasons are present. Most cavities close if left alone, and most cavities which do not close are asymptomatic. If incapacitating symptoms are present, however, then I would certainly use thoracotomy if phrenic crush failed to cure the patient."

Dr. Plimpton Guptill, Rochester, N. Y., said: "It is my feeling that surgery is not particularly appropriate in the cavitation of this disease. I believe they should have a long period of conservative treatment and that a decrease in the expansion of the lung by phrenic nerve is a safe procedure."

Dr. W. L. Rogers of San Francisco wrote: "We have used three types of resection: (1) Lobectomy, where considerable parenchymal infiltrate is present; (2) segmental resection; (3) enucleation or excision of the cavity itself, not attempting any repair of the parenchyma after it is excised."

Dr. David J. Dugan of San Francisco said this: "I feel it is safe to assume that, as far as resection in coccidioidomycosis is concerned, particularly with cavitation, excisional surgery is only indicated in the presence of pulmonary hemorrhage."

Dr. F. X. Byron, Los Angeles, stated: "From my knowledge of the disease in general, it would seem to me that segmental lobectomy should not be undertaken because of the possibility of traversing infective lung tissue, and, as you know, coccidioidomycotic empyemas are notoriously difficult to handle. Lobectomy, however, appears to be entirely feasible in most cases."

Dr. Lawrence Miscall, New York, says this: "I am convinced that in this disease one must be careful of the possible presence of disseminated foci. I know of no other way to reach a positive conclusion in regards to these foci than by taking postero-anterior and both lateral tomographic series."

Dr. Robert Shaw of Dallas, Texas, stated: "At present it is my opinion that granulomas caused by coccidioidal infection should be removed by excision. I also believe that residual cysts from this infection are best treated by excision. From the experience of others I have gained the impression that pneumothorax therapy or paralysis of the diaphragm will not bring about closure of these defects. We have found them to be epithelized in the cases in which we have removed the cysts, so that is readily understandable why these cysts will not heal with collapse."

Dr. John C. Jones of Los Angeles said: "It is my feeling that the incidence of complications in lobectomy at the present time is so low, and the mortality is so low, that certainly a persistent long-standing granulomatous cavity is an indication for a resection, and I believe that will probably be more or less accepted in the not too distant future."

Dr. Fred Harper of Denver had this to say: "I believe that only the very persistent cavities would be suitable for lobectomy."

Dr. Thomas Burford, St. Louis, wrote: "From what I can learn from my colleagues, I believe it is the general feeling that carefully done excisional surgery is the treatment of choice in the old, long-standing cases with recalcitrant cavities. A prime requisite of successful surgery is a wide excision of the disease-bearing area. For myself I would never do a segmental lobectomy in this disease."

Dr. W. A. Winn of Springville, Calif., said: "I am inclined to believe that surgeons are somewhat overdoing resection for this disease. Perhaps the indications for resection have to be more sharply defined. The existence of cavitation per se should not mean pulmonary resection, but under certain circumstances surgical removal does become necessary."

CONCLUSION

Excisional surgery has been carried out in 98 instances for pulmonary coccidioidomycosis. The indications are persistent cavitation, recurrent hemorrhage, productive cough, suspicion of neoplasm, granuloma, failure of the lung to re-expand following spontaneous pneumothorax, indeterminate lesions failing to respond to conservative measures, and residual cysts due to epithelization of previous coccidioidal cavity.

The complications have been few, but those recorded were empyema, bronchopleural fistula, and recavitation in the remaining portion of the lung. Three deaths following excisional surgery are reported.

ADDENDUM

Additional reports have brought the total number of cases of excisional surgery in pulmonary coccidioidomycosis to *one hundred nine*. An additional lobectomy plus a case of local excision should be credited to Greer, Forsee, Grow, and Mahon. Also, Dr. Bert Cotton should be credited with an additional 5 pneumonectomies, plus 4 in which local excision of the cavity was carried out. Dr. Cotton has this, in addition, to say in regard to surgery in this disease: “As far as reactivation in coccidioidomycosis is concerned, I have never seen this occur, and this includes an experience with over 500 cases I have reviewed. I feel it will never be necessary to do a postoperative thoracoplasty to prevent reactivation. I have never seen this disease, when in the chronic phase, spread in the manner of tuberculosis. Dr. Byron mentioned how difficult it was to handle empyema from coccidioidomycosis. I might state that in 4 decortications the surgery was performed in the presence of purulent material, and this purulent material was filled with spherules of coccidioidomycosis. These 4 decortications were accomplished, and the postoperative course of the patients was characterized by freedom from complication. One discussant mentioned that excisional surgery is only indicated in the presence of pulmonary hemorrhage. In several cases I have found secondary suppurative infection in the cavities, and this is considered an indication for pulmonary resection. As far as segmental foci are concerned, in every case upon which I have operated for cavitation, many small foci were palpated in the adjacent lung, but were completely disregarded as being unimportant as to reactivation. I would also like to take exception with Dr. C. E. Smith’s statement that most cavities close if left alone. If he is speaking of the acute cavity, then he is correct; however, if he is talking of the chronic cavity which persists after the acute infection has disappeared, then he is speaking of the cavities which we are trying to eliminate with collapse therapy and resection, and they do not close spontaneously. The statement that most cavities that do not close are asymptomatic we have found to be incorrect.”

CYSTIC ACCESSORY LOBE

REPORT OF A CASE

LEON J. LEAHY, M.D., AND JAMES D. MACCALLUM, M.D.
BUFFALO, N. Y.

A RECENT patient with cystic disease of the lung presented a type of this condition which was unique in our experience. After reviewing the literature and discussing the condition with several other thoracic surgeons, it would appear that this variety justifies the following case report.

J. C., a white man, 36 years of age, occupation, laborer, was admitted to the Buffalo General Hospital on Nov. 19, 1948. Chief complaint was of pain in the left lower chest of about two weeks' duration. The onset of pain occurred while he was carrying a heavy weight. It first appeared in the left shoulder and five days later the pain recurred in the left lower chest. This was not severe and only slightly aggravated on deep inspiration. On inquiry, a history of an unproductive cough of six months' duration was elicited. Functional inquiry and laboratory examinations were negative.

Physical examination showed a rather asthenic man, 6 feet 6 inches tall, not acutely ill. The only positive physical findings were in the left chest in which area flatness to percussion and absent breath sounds were present in the lower third.

He was referred to the hospital because it was felt he was suffering from spontaneous pneumothorax following x-ray films made elsewhere. Bronchoscopic examination revealed a normal tracheobronchial tree.

X-ray studies of the chest, fluoroscopically and radiologically, revealed a huge intrapulmonary cystic structure in the left chest. The cyst wall touched the anterior pleura and very closely approximated the diaphragm, which was elevated. It was in contact with the left lateral chest. There was a considerable amount of fluid in the left pleural space. However, none could be demonstrated within the cyst. The heart was deviated to the right. It was difficult to localize which portion of the lung contained the cyst and in positioning the patient to determine this fact, it was found that the location of both pleural fluid and the air-filled cyst seemed to move about with great freedom. This phenomenon aroused our curiosity and we were somewhat at a loss to explain the mechanism through which it occurred.

Final x-ray and clinical diagnosis of pulmonary cyst in the lower portion of the left upper lobe with a bronchial communication and associated with a pleural effusion was arrived at. Lobectomy was decided upon.

Operation.—On Nov. 23, 1948, a thoracotomy was done under intratracheal anesthesia, with resection of the sixth rib on the left side. There was a moderate amount of cloudy fluid in the pleural cavity. This was estimated at 300 c.c., cultured, and proved to be sterile. There was no evidence of tuberculosis. The lower lobe was markedly collapsed, being practically airless, and the upper lobe showed a lesser degree of atelectasis. The striking finding of a large cyst bulging through the wound after the pleura was opened was encountered. This was thin walled, filled with air, and the size of a fetal head. It could be moved about with great freedom and on inspection of the pleural cavity, it was found to originate from the pulmonary ligament, completely below the left lower lobe, and not attached to any other structures except the ligament. It was unilocular and there was

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found to be a fairly small pedicle by which it was connected with the mediastinum. It very closely resembled a large ovarian cyst, attached to the broad ligament by a narrow stalk at the base. When positive pressure was applied by the anesthetist, the shape or tension of the cyst was not affected. This was in spite of the fact that there was a small, goose-quill like bronchus entering it. It was a very simple matter to apply two clamps, remove the cyst, and ligate the pedicle. Following the removal of the cyst, both lobes expanded fully under positive pressure, and the chest wall was closed.

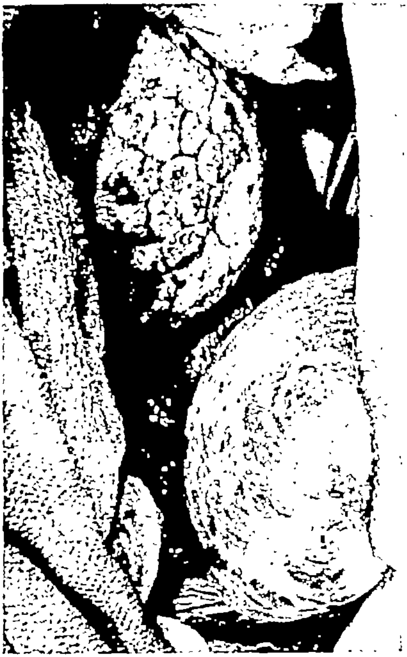

Fig. 1.—The cyst is in the lower field. The atelectatic lower lobe lies deep in the chest. Above it the normal upper lobe is seen.

The patient's postoperative course was entirely benign and he was discharged on Dec. 2, 1948, without chest fluid and the lung fully expanded. Follow-up film taken March, 1949, revealed no abnormalities.

Pathology Report.—The pathologic report* was of a pear-shaped cyst with a very thin wall, measurements 13 by 10 cm., filled with air. A few c.c. of bloody fluid shone through the wall. The cyst in a fixed state contained about 20 c.c. of hemorrhagic fluid but otherwise only air. It could be probed through a channellike structure which appeared compressed in semilunar fashion and apparently contained cartilage in the wall. The hilar portion for a distance of about 2.5 cm. consisted largely of lunglike tissue and the cystic channel about 1 cm. in diameter leading to the large cyst.

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*By Dr. Kornel Terplan.

Microscopic sections through the cyst showed a considerably hyalinized wall and in numerous areas a well-preserved epithelial lining consisting of cuboidal and low columnar forms. There was no cartilage, nor were there any mucous glands in the wall. The pleural part was considerably thickened and moderately infiltrated by lymphoid cells. Sections through the hilar portion showed a lobular lung pattern with distended alveolar spaces most of which showed an epithelial lining similar to the large cyst. Throughout the septa there was an accumulation of lymphoid cells and scattered eosinophils. Within the alveolar spaces was recent blood. Part of the stroma within the hilum was markedly edematous.

Conclusion.—The entire structure was actually an additional anlage of a pulmonary lobe with huge cystic distention of one or more original alveolar or bronchiolar spaces.

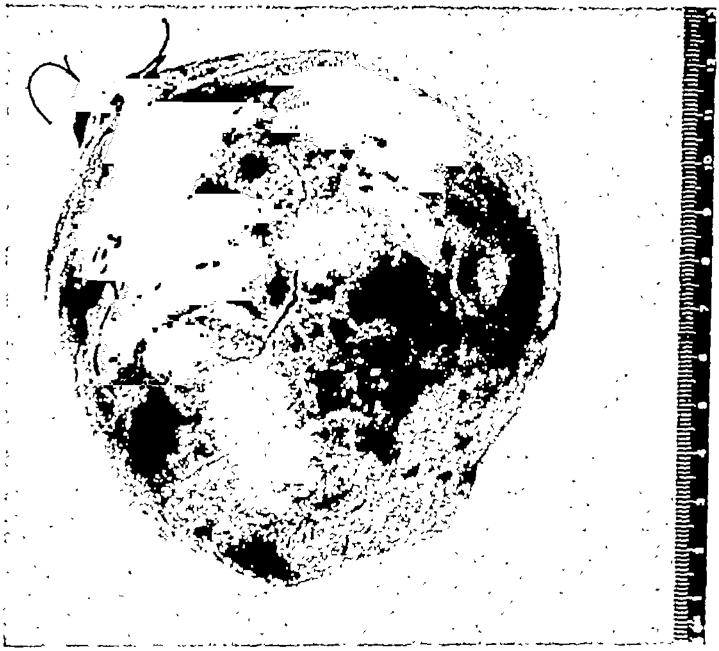

Fig. 2.—Surgical specimen.

DISCUSSION

Accessory lobes have been recognized since 1687, but in 1925, Koontz[1] was able to collect only 108 cases. Since that time at least several hundred more have been added, so that the condition is now well recognized. Freedlander and Gebauer[2] suggested that this anomaly occurs when tracheal buds push into the mesenchyme and become partially isolated. In some cases the communication with the tracheobronchial tree remains so that an accessory lobe is produced in contradistinction to the aberrant lobe in which there is no communication.

Cystic change in an accessory lobe was found by Koontz[1] in four cases. Tyson,[3] Anzola-Carillo,[4] and Santy, Berard, and Galy[6] have reported cases in which fluid contents were present in the cyst. The presence of a pedicle was uncommon. Kleine[5] described a post-mortem specimen in which a thin-walled air-filled cyst was connected to the medial portion of the left upper lobe by a pedicle. The development of cystic change is not well understood although bronchial obstruction due to stenosis, retained secretions, or valvular formation due to faulty

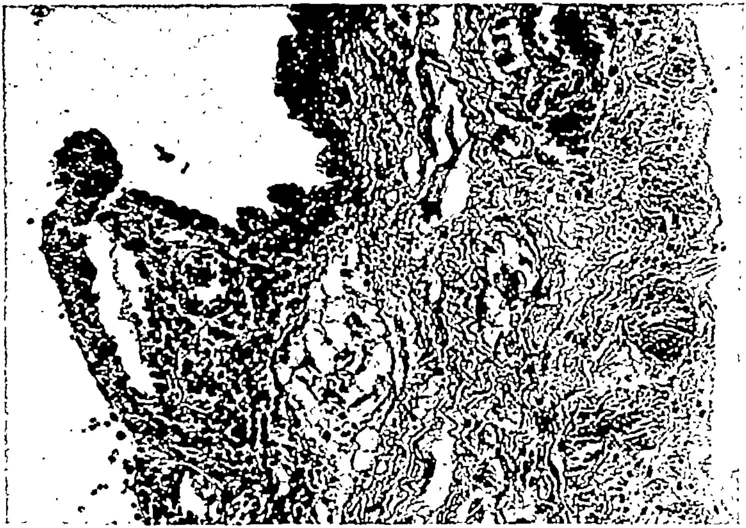

Fig. 3.—Cyst wall showing columnar epithelial lining.

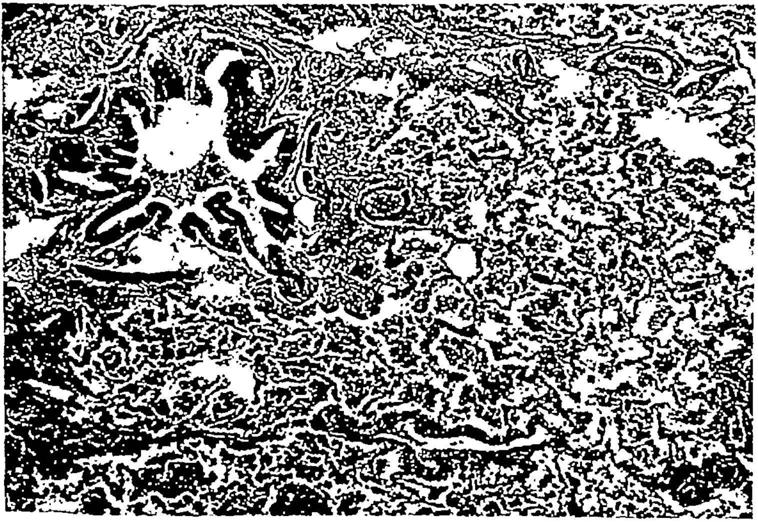

Fig. 4.—Hilar portion of the cyst.

canalization has been suggested. If such obstruction occurs in a higher order bronchus or bronchiole distal to mucous glands, it would be air-filled as in the case presented.

Clinically, Santy, Berard, and Galy,[6] feel that it is difficult to make a clinical diagnosis of cysts of the pulmonary pedicle. Alterations of positions will cause pain, clicks, and vasomotor disturbances, due to the pull of the cyst. This was not present in our case quite possibly due to the fact that the cyst was air-filled and did not, therefore, exert much traction. These authors feel that all cysts having their origin in the region of the pulmonary pedicle arise from an accessory bronchial bud or from a supernumerary lobe. They report four cases which fall in this group; in all of these the cysts contained fluid. These authors mention only two cases in the literature in which air also was present in the cyst so that a fluid level was visible.

A lesion such as the one reported may be confused with a pneumothorax. Adequate x-ray study in various positions will indicate that the air is contained within a cystic wall. In this instance free pleural fluid offered an additional means of differentiation.

Surgical excision is the only satisfactory treatment. Removal of these lesions avoids the hazards of infection, the effects of continued growth, and the possibility of malignant change. Theoretically at least, it is possible for cysts of this type to undergo torsion of the pedicle and subsequent necrosis. These cysts may be removed without sacrifice of pulmonary tissue.

Addendum.—Since this article was submitted for publication the report of a somewhat similar case has appeared in the literature: DeBakey, M., Arey, J. B., and Brunazzi, R.: Successful Removal of Lower Accessory Lung, J. THORACIC SURG. 19: 304-312, 1950.

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RHABDOMYOSARCOMA OF THE ESOPHAGUS

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RHABDOMYOSARCOMA of the esophagus is an extremely rare lesion. Only 3 cases could be found in the world literature, and we are adding a fourth. As far as we could determine, our case is the only rhabdomyosarcoma which was *resected, the patient being alive and apparently well one year after surgery.*

REVIEW OF THE LITERATURE

After a very thorough study of the world literature we were able to collect 58 proved cases of sarcoma of the esophagus. Of this group 30 were fibrosarcomas, 8 were leiomyosarcomas, 5 were lymphosarcomas, 5 were melanosarcomas, 7 were unclassified sarcomas, and only 3 were rhabdomyosarcomas (Table I).

Chapman (1877)[1] described the first esophageal sarcoma. This lesion arose from the inferior constrictor muscle of the pharynx and the inlet of the esophagus. He stated that "it may be considered to belong to the comparatively innocent sarcomas, death having been produced rather from the accident of its situation rather than from the violence of its constitutional effects." Starck (1900)[2] collected 7 cases of sarcoma of the esophagus from the literature and added 2 of his own. Corner and Fairbank (1904)[3] reported 14 cases of sarcoma of the esophagus. Hacker (1909)[4] collected 21 cases of esophageal sarcoma, but later Hacker and Lotheissen (1926)[5] stated that 38 cases had been described, but that in some of these the origin was doubtful. Goldstein (1921)[6] collected 21 cases of proved sarcomas. Fischer (1926)[7] found 50 reported cases, but Simon (1928)[8] stated that there were only 30 objection-free cases in the literature. These statements need only to be read to appreciate the state of confusion which exists regarding the incidence of this condition.

Sarcoma of the esophagus occurs more frequently in men and has been found in ages ranging from 4 to 70 years.[9] However, more sarcomas were seen in the early age group than were carcinomas.

Rhabdomyosarcomas are found most frequently in the genitourinary system, namely, the uterus, vagina, testis, bladder, and particularly in the kidney. The congenital lesions of this type of tumor are frequently found in the heart. These tumors have also been reported in the tongue, stomach, parotid gland, breast, prostate gland, and practically all the voluntary muscles of the body.[9] The occurrence of rhabdomyosarcoma in the esophagus, however, is a rarity, such a lesion having been reported, as stated previously, only 3 times before; our case is the fourth on record.

The 3 cases previously described as rhabdomyosarcoma of the esophagus were recorded by Wolfensberger,[10] Glinski,[11] and Dvorak.[12] Wolfensberger

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TABLE I. PRIMARY ESOPHAGEAL SARCOMAS REPORTED IN THE LITERATURE

AUTHOR	DATE	TYPE OF SARCOMA	NUMBER OF CASES CITED	CLASSIFICATION
E. Chapman[1]	1877	Spindle, round, and oval cells	1	Fibrosarcoma
J. H. Targett[26]	1888-1889	Spindle, round, and oval cells	1	Fibrosarcoma
B. H. Stephan[27]	1890	Sarcoma of lymphocytic origin	1	Lymphosarcoma
L. Shaw[28]	1891	Round and oval cells	1	Fibrosarcoma
H. D. Rolleston[29]	1892-1893	Round cell	1	Fibrosarcoma
R. Wolfensberger[10]	1894	Striated muscle cells	1	Rhabdomyosarcoma
A. Notthaft[30]	1895	Spindle cell	1	Fibrosarcoma
Albrecht[31]	1895	Alveolar sarcoma	1	Fibrosarcoma
C. Ogle[32]	1896	Spindle cell	1	Fibrosarcoma
L. E. Livingood[33]	1898	Spindle cell	1	Fibrosarcoma
G. B. James[34]	1898	Spindle cell	1	Fibrosarcoma
H. Starck[2]	1900	Round, oval, and spindle cells	1	Fibrosarcoma
		Round, oval, and spindle cells	1	Fibrosarcoma
A. Gastpar[13]	1900	Large mixed cell: spindle and round cells	1	Fibrosarcoma
T. Chiba[35]	1900	Mixed cell	1	Sarcoma (unclassified)
L. Huismans[36]	1901	Round cell	1	Fibrosarcoma
L. K. Glinski[11]	1902	Mixed tumor with striated muscle	1	Rhabdomyosarcoma
C. von Eicken[24]	1902	Spindle and giant cells	1	Fibrosarcoma
W. T. Howard, Jr.[37]	1902	Smooth muscle cell	1	Leiomyosarcoma
E. H. Bauer[14]	1904	Pigmented tumor cells	1	Melanosarcoma
Wegener[38]	1904	Round cells	1	Fibrosarcoma
Von Lange[39]	1904	Spindle and large round cells	1	Fibrosarcoma
P. Frangenheim[40]	1906	Spindle and giant cells	1	Fibrosarcoma
H. Joliat[41]	1907	Pigmented tumor cells	1	Melanosarcoma
V. Hacker[4]	1908	Spindle cells and smooth muscle cells	1	Leiomyosarcoma
K. Donath[42]	1908	Spindle and giant cells	1	Fibrosarcoma
G. Herxheimer[43]	1908	Spindle cells	1	Fibrosarcoma
R. Borrmann[44]	1908	Spindle and giant cells	1	Fibrosarcoma
J. W. Reith[45]	1909	Giant cell type	1	Fibrosarcoma
		Giant cell type	1	Fibrosarcoma
Rieke[46]	1909	Spindle and giant cells	1	Fibrosarcoma
Snoy[47]	1911	Mixed cell	1	Sarcoma (unclassified)
E. Bertholet[48]	1911	Round cell of lymphocytic origin	1	Lymphosarcoma
Schmincke[49]	1914	Mixed cell	1	Sarcoma (unclassified)
C. Jackson[50]	1915	Round cells	1	Fibrosarcoma
E. Bauer[51]	1916	Smooth muscle cells	1	Leiomyosarcoma
M. Hofman[52]	1920	Pigmented spindle cells	1	Melanosarcoma
C. Jackson[53]	1925	Round cells	1	Fibrosarcoma
		Lymphocytic origin	1	Lymphosarcoma
V. Hacker and G. Lotheissen[5]	1926	Round and spindle cells	1	Fibrosarcoma
M. Schwartz[54]	1926-1927	Spindle cells	1	Fibrosarcoma
J. Guisez[55]	1927	Undifferentiated cells	1	Sarcoma (unclassified)
A. M. Martin[56]	1928	Lymphocytic origin	1	Lymphosarcoma
K. Matsuoka and H. Hata[57]	1928	Undifferentiated cells	1	Sarcoma (unclassified)
E. Voss[58]	1928	Pigmented tumor cells	1	Melanosarcoma
H. J. Dvorak[12]	1931	Striated muscle cells	1	Rhabdomyosarcoma
R. Waldapfel[59]	1932	Undifferentiated cells	1	Sarcoma (unclassified)
T. B. Mallory[60]	1935	Smooth muscle cells	1	Leiomyosarcoma
T. C. Jaleski and P. V. Waldo[61]	1935	Pigmented tumor cells	1	Melanosarcoma
C. Jackson[62]	1935	Lymphocytic origin	1	Lymphosarcoma
		Round cells	1	Fibrosarcoma
		Spindle and round cells	1	Fibrosarcoma

TABLE I—CONT'D

AUTHOR	DATE	TYPE OF SARCOMA	NUMBER OF CASES CITED	CLASSIFICATION
F. R. Menne and R. F. Birge[63]	1937	Spindle and oval cells in striated muscle	1	Leiomyosarcoma
L. R. French and L. H. Garland[32]	1941	Smooth muscle cells	1	Leiomyosarcoma
L. Bayer[64]	1941	Undifferentiated cells	1	Sarcoma (unclassified)
A. E. Penner[65]	1942	Smooth muscle cells	1	Leiomyosarcoma
Case No. A 361 of the University of Texas[66]	1949	Smooth muscle cells	1	Leiomyosarcoma
D. E. Clark[67]	1949	Connective tissue cells	1	Fibrosarcoma
P. Thorek and B. Neiman	1949	Striated muscle cells	1	Rhabdomyosarcoma
Total			59	

(1894)[10] reported a case of primary rhabdomyosarcoma of the lower third of the esophagus. Associated with this lesion was a metastasis to a gland behind the cardiac end of the stomach. Microscopic studies revealed cross striations. He interpreted the cellular elements of this tumor, other than the muscle present, as undifferentiated embryonal cells. Glinski (1904)[11] stated that the cells were types which differentiate into entirely different tissue and therefore called the growth in his case a mixed tumor with striated muscle. He was of the opinion that these tumors arise from undifferentiated mesenchyme which becomes displaced when the developmental changes occur in the ventral floor of the foregut, and that cross striations in the muscle cells of these tumors are difficult to demonstrate and find. Dvorak's[12] case was found in the cervical region of the esophagus in a woman 27 years old. Although cross striations could not be demonstrated by him, this was believed to be due to a failure of fixation of the fresh tumor tissue in a proper solution. He believed, however, that the embryonal cells which he demonstrated were differentiating into striated muscle of the voluntary type.

The tumor in our case, which shall be described subsequently, was examined microscopically by one of us (B. N.), and also by the Army Institute of Pathology. Both agreed that "this lesion is undoubtedly a myosarcoma, and that the most likely possibility is a rhabdomyosarcoma." It has been coded in the Army Institute of Pathology as a rhabdomyosarcoma.

PATHOLOGY

Sarcoma of the esophagus is found most frequently in the lower part of the thoracic esophagus, and like carcinoma selects the three esophageal constrictions as the points of predilection. The lesion may be quite small as in Dvorak's[12] case, or may be very large as in the cases reported by Gastpar[13] and Bauer.[14]

Esophageal sarcomas have been classified by Ewing[9] into the following two groups: ulcerative growths and polypoid growths. Kaufman,[15] Hacker and Lotheissen,[5] and Fischer[7] preferred to group these lesions as: (1) the more circumscribed type, and (2) the diffuse infiltrating type.

Sarcoma, especially of the circumscribed polypoid variety, usually arises from the anterior wall of the esophagus and from its submucosa.[16]

Spindle-cell sarcomas of the polypoid variety grow slowly and produce only little tissue destruction. The infiltrating and ulcerating round-cell type grow rapidly and may obstruct the lumen. This type may ulcerate and produce hemorrhage, necrosis, and/or perforation.

Metastases occur more frequently in the diffuse infiltrating type of round-cell sarcoma (ulcerative type). On the other hand, in the spindle-cell sarcomas (polypoid type) metastases are usually lacking.

Carcinosarcoma is a difficult lesion to comprehend and understand. However, such cases have been reported by Herzog,[17] Saltykow,[18] Socin,[19] Pratt and Lockyer,[20] and Sokolov.[21] These lesions, as suggested by Ewing,[9] are probably undifferentiated carcinomas with a very reactive stroma and consequently are not included in this review.

On July 28, 1948, two pieces of tissue were submitted to surgical pathology. The larger piece measured 4 by 2 by 2 mm. and the smaller 1 mm. in diameter. On microscopic examination, the larger piece showed esophageal mucosa with some inflammatory reaction. The other piece was composed of degenerated inflammatory tissue in which large irregular polygonal cells were seen with deeply staining irregular nuclei. On this cytologic appearance, the diagnosis of a squamous-cell carcinoma was made. This error in biopsy diagnosis was also mentioned by French and Garland[22] in their case. A larger biopsy from the lesion would perhaps have prevented this error in diagnosis. The correct diagnosis of rhabdomyosarcoma was made from the resected specimen.

DIAGNOSIS

Although the symptoms may resemble those produced by carcinoma, certain differences have been noted which will be discussed presently. The most common symptom is dysphagia; this usually occurs early and may completely obstruct the esophageal lumen. This symptom progresses slowly and in the typical stereotyped fashion, the patient changes the type of diet from solids to semisolids to liquids. As a rule the patient can accurately demonstrate at which point the food sticks. Salivation and regurgitation of undigested food particles have also been rather common complaints. Pain is usually an early symptom. Simon[8] is of the opinion that its early appearance, piercing character, and radiation between the scapulae are characteristic. The pain in sarcoma seems to appear in attacks which occur at night and may not be related to the intake of food. Abel[23] believed that the pain was due to the dilatation of the esophagus above the lesion; this is associated with increased muscular contractions of the organ. Cachexia makes its appearance early and von Eicken[24] was of the opinion that this early cachexia was associated with loss of sleep at night. Anemia may be present because of the slow but constant loss of blood, or the hemorrhage may be massive as in Dvorak's[12] case in which instance a black stool was reported. The condition may be confused with pulmonary afflictions or aneurysms because of the encroachment of the primary lesion upon the surrounding structures.

It is difficult, however, to differentiate sarcoma from carcinoma of the esophagus. The following factors may be helpful although the final diagnosis is made only after careful microscopic study. When the degree of wasting is out of proportion to the degree of dysphagia a sarcoma should be suspected rather than a carcinoma. Malignant appearing lesions of the esophagus in patients under the age of 30 years are usually sarcoma and not carcinoma. Sarcomatous lesions have a tendency to be more polypoid and pedunculated, whereas the carcinomas are more infiltrative in type and irregular. The pain in carcinoma is most marked after eating; however, as stated, the pain in sarcoma may be present while fasting. The duration of the disease in sarcoma is shorter than in carcinoma since the former runs a more rapid and fatal course, and metastasizes earlier.

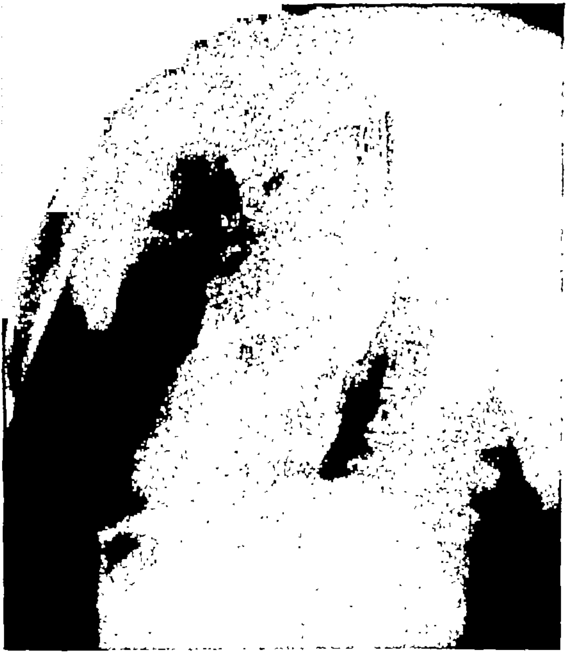

Fig. 1.—Preoperative x-ray film, lateral view, of the esophagus in the case herein described.

The prognosis of carcinoma is somewhat better than that of sarcoma, since the latter progresses with such marked rapidity. Death is usually associated with starvation, and has also been reported from perforation into adjacent organs (mediastinitis, lung abscess, tracheal perforation, or hemorrhage). The patient rarely lives longer than six months after the onset of dysphagia.

TREATMENT

With modern advances in anesthesiology, chemotherapy, and improved surgical technique, especially following the teachings of Sweet and Garlock, surgical therapy has greatly increased its scope and safety. These patients today, therefore, are given a new lease on life, and if nothing else, palliative resections and anastomoses can prevent a lingering death of starvation and thirst.

Nielsen[25] has attempted to treat carcinoma of the esophagus by means of rotatory irradiation with the patient seated. How this type of rotation x-ray therapy will affect sarcomatous growths, which should be more radiosensitive than carcinoma, will only be told in the course of time.

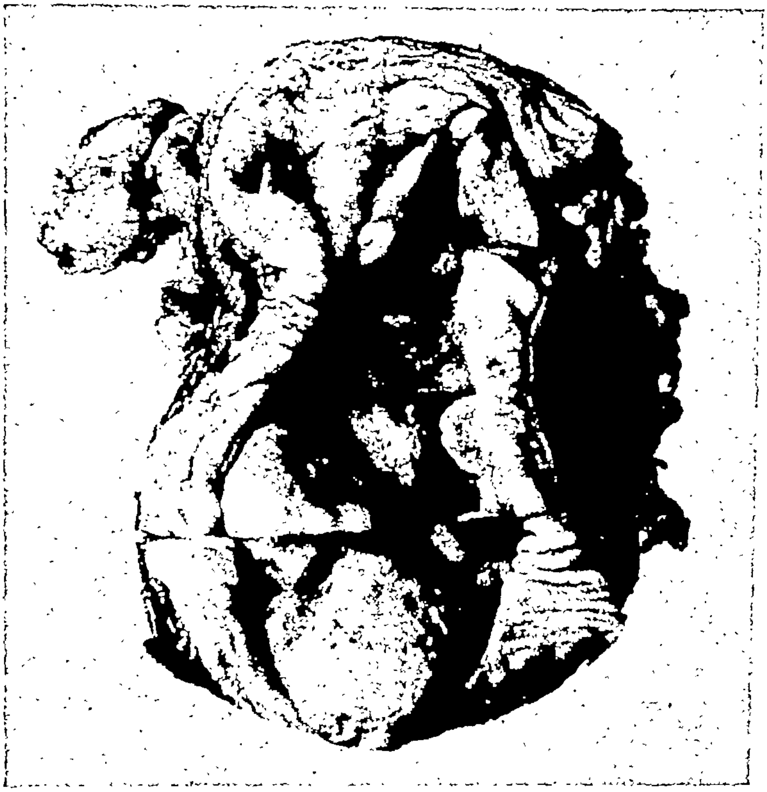

Fig. 2.—A photograph of the gross specimen. The polypoid appearance and the free margin of the tumor are readily seen.

In 1939, Dvorak[12] wrote, "the operative treatment for sarcoma in the thoracic esophagus offers little prospect of success. No successful case was found reported." In only a short span of time this statement surely has become outmoded.

Unfortunately, the three other cases of rhabdomyosarcoma did not have the benefits of modern surgery. Our patient is alive and well one year following partial esophagectomy with transthoracic supra-aortic esophagogastrostomy.

CASE REPORT

History.—The patient, J. P., male, aged 43 years, was admitted on July 27, 1948, with a complaint of dysphagia and repeated vomiting for 3 months. The patient stated that he was perfectly well until 2 months prior to admission, when he was suddenly seized by an attack of vomiting after eating a rather hearty meal. Prior to this he could not recall having any similar attacks or difficulty in swallowing. Since the date of the first attack, difficulty in swallowing progressed rapidly so that within a period of 2 weeks he could only swallow liquid foods. He was extremely nauseated and repeatedly vomited following the intake of foods and liquids. The vomitus consisted of any semisolids previously taken. He had dropped in weight from 135 to 124 pounds within a period of 8 weeks. He complained of marked weakness and dizziness. Four weeks prior to entrance he began to complain of a substernal aching which was referred to the region of the shoulders. Previous history revealed a rather excessive intake of alcohol over a period of many years. An appendectomy had been performed 8 years prior to entrance.

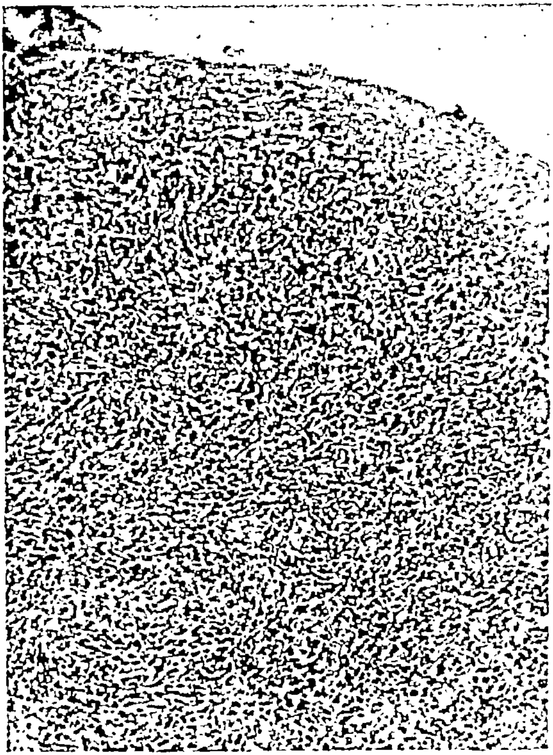

Fig. 3.—Microscopic appearance of the tumor (magnification, ×150). The gradual thinning of the esophageal mucosa with its entire absence over the tumor is clearly demonstrated.

Physical Examination.—Physical examination revealed an emaciated man with a normal temperature, pulse and respiration; blood pressure was 120/60. Physical findings were essentially normal.

X-ray Examination.—An esophagogram revealed a filling defect in the thoracic esophagus slightly below the arch of the aorta. There was slight dilatation of the esophagus above the lesion, and only a trickle of the barium could proceed into the stomach (Fig. 1).

The esophagoscopist reported the appearance of a gray, piled-up, granular lesion 27 cm. from the lower alveolar margin. This bled easily. A biopsy of this tissue was reported as squamous-cell carcinoma of the esophagus. (This has been commented upon previously.)

Although the patient's mechanical symptoms were well marked, he maintained a red blood cell count of 4,190,000. The patient was prepared for surgery by means of proper protein, blood, electrolyte, water, and vitamin balance.

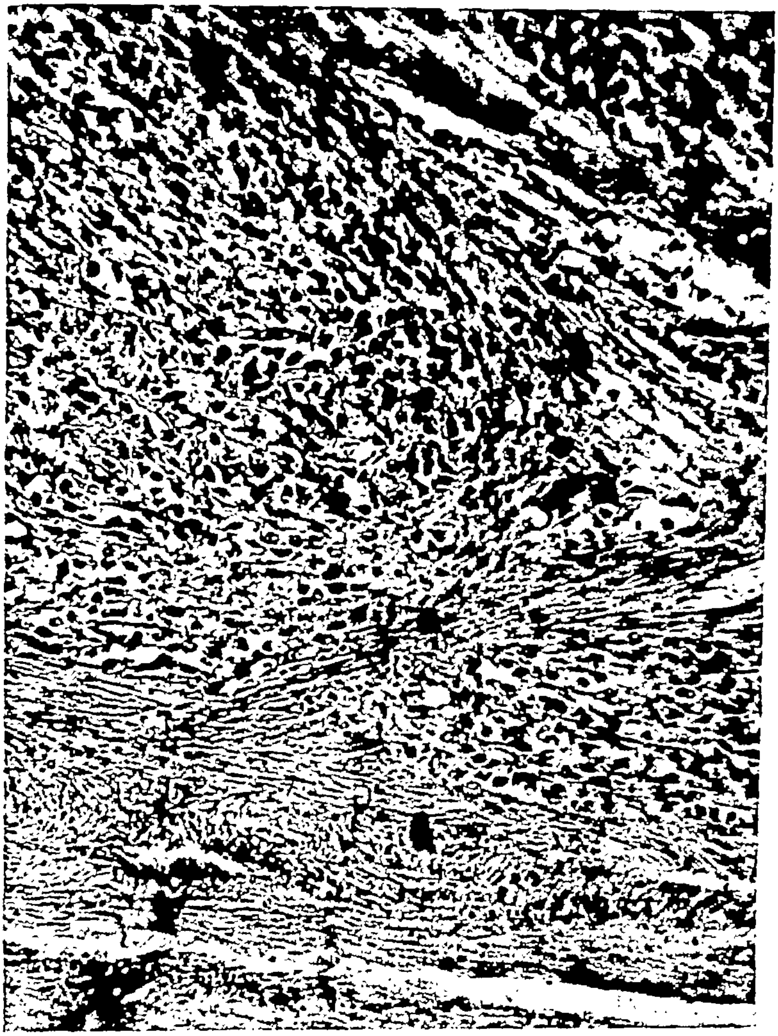

Fig. 4.—Microscopic appearance of the tumor (magnification, ×250). Note the pleomorphic structure of the cells with giant forms denoting its striated muscle-cell origin.

Treatment.—The patient was operated upon on Aug. 4, 1948, by one of us (P. T.), utilizing a standardized technique of supra-aortic esophageal resection.[68] The incision extended from the sixth costal cartilage anteriorly over the sixth rib and then up along the vertebral border of the scapula to the level of the third rib posteriorly. The sixth rib was resected subperiosteally, and the fourth, fifth, and seventh ribs were divided posteriorly. This gave ample exposure to the left thoracic cavity. The inferior pulmonary ligament and mediastinal pleura were incised. The esophagus was freed from the arch of the aorta to the diaphragm by severing its aortic and inferior phrenic blood supply. The lesion was freed from the surrounding structures below the arch of the aorta. This was accomplished by blunt dissection. The left hemidiaphragm was opened from the esophageal hiatus radially toward its peripheral attachment. The stomach was mobilized by severing and ligating the left gastroepiploic artery, the vasa brevia, and the left gastric artery. The blood supply to the stomach was well maintained by the right gastroepiploic and the right gastric arteries which remained intact. The supra-aortic mobilization of the esophagus was accomplished by incising the pleura immediately behind the left subclavian artery. The esophagus was then severed at the gastric cardia. The open stomach end was closed and inverted by two layers of sutures. The opposite end of the esophagus was tied off.

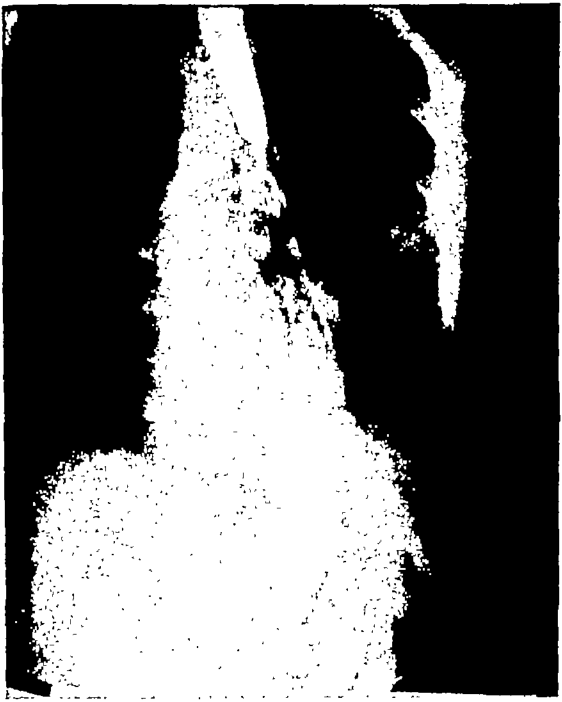

Fig. 5.—One year postoperative x-ray film, anteroposterior view, of the same patient, showing a well-functioning intrathoracic esophagogastrostomy.

The completely mobilized esophagus was readily removed from its mediastinal bed and brought over the arch of the aorta. The mobilized stomach was now displaced high into the thoracic cavity, passing between the pulmonary hilum and the arch of the aorta. Partial esophagectomy was performed followed by a supra-aortic esophagogastrostomy using two layers of sutures. A Levine tube passed through the nose remained in the stomach with constant suction attached. The pleural cavity was drained through an incision in the ninth intercostal space, and the catheter placed under water-seal drainage. The wound was closed in the conventional manner. The operation lasted 3 hours and 50 minutes, and 1,500 c.c. of blood was used throughout the procedure.

Pathologist's Report.—Macroscopic specimen: On Aug. 4, 1948, a portion of the esophagus was submitted to the laboratory. It measured 7 cm. in length and 3 cm. in diameter.

The surface was smooth. On opening into the lumen a mass presented itself having a pear or tonguelike shape. It was slightly polypoid in character and measured 3½ by 2½ by 2 cm. (Fig. 2). The surface showed an absence of mucosa and was a dirty brown gray. The mass was firm in consistency, the edges raised and rolled. The mucosa of the esophagus below and above the lesion was pinkish tan and smooth. The thickness of the esophageal wall was 9 mm. On sectioning through the tumor mass it was 2 cm. in thickness and gray tan.

Microscopic description: The squamous epithelium adjoining the tumor showed a gradual thinning out to complete absence over the tumor (Fig. 3). The tumor itself was composed of elongated large cells. The nuclei were irregular and hyperchromic. Many mitotic figures were seen. There was a marked pleomorphism of the cellular elements and connective tissue stains revealed prolongations of cytoplasm with the stroma (Fig. 4). Some cells were giant types with large irregular deeply staining nuclei. Cross striations were not found with various staining techniques. A diagnosis of myogenic sarcoma was made with the histologic picture of a rhabdomyosarcoma.

Fig. 6.—The patient one year after surgery.

The same specimen was submitted to the Army Institute of Pathology in Washington. They stated that "this lesion is undoubtedly a myosarcoma and that the most likely possibility is a rhabdomyosarcoma. We are coding the case under this diagnosis and will consider this our final diagnosis." After careful consultation, one of us (B. N.) concurred in this diagnosis, and felt that there was no room for doubt.

Glinski[11] and other investigators have stated that cross striations in the voluntary *muscle-cell tumors are very difficult to demonstrate and many times cannot be found,* especially when the tumor process is very undifferentiated.

An additional point of interest in this particular case is the presence of a striated muscle-cell tumor in a smooth muscle zone. To explain this is difficult and one can only theorize in that this was either a metaplasia or an embryonic arrest.

Postoperative Course.—The postoperative course was stormy for the first 2 days; however, following this it was quite uneventful. Both the Levine tube and the thoracic catheter were removed on the third postoperative day. The patient was permitted to walk at this time. Liquid feedings were started on the fourth postoperative day, and he was discharged on the sixteenth postoperative day. A very thorough course of postoperative x-ray therapy was outlined for the patient. He had one treatment; he refused to return for future x-ray therapy. His radiation therapy, therefore, cannot be considered as part of the postoperative treatment.

The postoperative roentgenogram taken one year following surgery revealed a well-functioning esophagogastrostomy (Fig. 5).

It is now a little over one year since this patient was operated upon. He has gained thirty pounds and is back at work, performing his usual duties and enjoying a full diet (Fig. 6).

SUMMARY

1. The subject of rhabdomyosarcoma of the esophagus is discussed, and a review of the literature is presented.

2. A case is herein described in which a striated muscle malignant neoplasm was found to be present in a zone of the esophagus where normally only smooth muscle is situated. Theories explaining this are discussed.

3. *This is the first known case in the world literature* in which a rhabdomyosarcoma of the esophagus was successfully removed. The patient is alive one year following surgery.

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EFFECTIVENESS OF DROMORAN (3-HYDROXY-N-METHYL MORPHINAN*) AS AN ANALGESIC IN THORACIC SURGERY

Preliminary Report

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THIS clinical study was undertaken to evaluate the analgesic effectiveness of Nu-2206 and compare it with others commonly employed for this purpose. The need for better analgesia is universally recognized since drugs presently prescribed often only partially control pain (demerol), frequently create undesirable side reactions as nausea, vomiting, respiratory depression, etc. (morphine), and are frequently short acting.

Following thoracic surgery the desirability of complete pain relief is of even greater importance. Here the wide division of muscles and pleural irritation sets up such intense pain that the patients find it difficult or impossible to perform the routine stir-up regimen. Their inability to cooperate may lead to atelectasis. In order to avoid such complications it is not uncommon to observe the nurses on a thoracic service forcefully and vigorously putting patients through the stir-up exercises of deep breathing, turning them from side to side, and encouraging coughing and expectoration. Any analgesic permitting freedom from pain, and at the same time having a minimum of undesirable side effects, would be of inestimable value to both patients and thoracic teams.

Nu-2206 is a synthetic morphinelike drug with a chemical formula of 3-hydroxy-N-methylmorphinan-hydrobromide.[1] Its close chemical relationship to morphine is readily observed in Fig. 1. It is a colorless, crystalline material readily soluble in water and alcohol. Pharmacologically, other workers have shown in mice and rats that Nu-2206 has a wide range of safety between its effective analgesic dose and the minimal lethal dose (Therapeutic Index).[2] In this respect it compares less favorably than dilaudid, favorably with morphine, and is superior to amidone and demerol. In man the effective dose for pain relief has been shown to be 5 mg. However, individuals without pain may develop marked respiratory depression with as little as 3 mg. This consideration must always be kept in mind before the drug is administered.

Pain relief can be determined either by checking directly with the patient the duration and amount of analgesia, or by obtaining from the nurses' records the daily number of hypodermics. The latter approach is undesirable and inaccurate for several reasons. First, unless requested by the medical staff a nurse in our hospital is in no position to offer a narcotic in less than 3 or 4 hours. During this period the patient may have little or no pain relief. Second, since some patients can tolerate a certain amount of pain for a period beyond

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*Made available for experimental purposes through the courtesy of Hoffmann-La Roche, Inc., Nutley, N. J. This drug was formerly known as "Nu-2206."

4 hours, the nurses withhold hypodermics until requested. Thus, a considerable discrepancy may exist between the period of actual pain relief and the interval between administration of hypodermics. Actually, in many instances, intervals of three to four hours were noted between the time of pain recurrence and the need for a hypodermic. In order to avoid errors patients were questioned as to the duration and extent of pain relief.

In addition to pain relief, patients were also observed for their ability to cough and expectorate easily and effectively, breathe deeply, and turn their body without pain. Complications were recorded. There was but one case of atelectasis in this entire series. Unquestionably, more would have developed had those individuals with minimal or no pain relief been spared from active routine stir-up regimen. In such cases this regimen was performed despite protestations of the patient. Finally, any change in judgment or insight was noted.

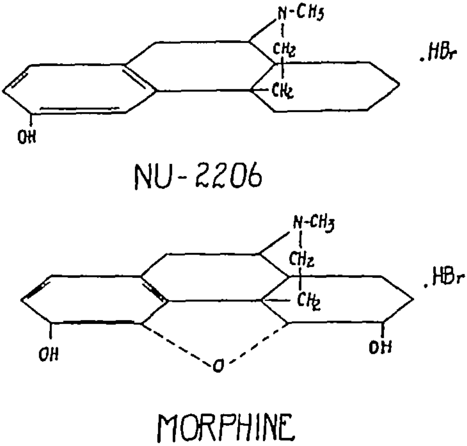

Fig. 1.—Showing close structural relationship between Nu-2206 and morphine.

Our study included a total of 67 patients. Fifty-seven cases had single-stage surgical procedures which included pulmonary resections, decortications, coarctations of the aorta, patent ductus arteriosus, and thoracoplasties. Approximately one-half (28 cases) received 5 mg. of Nu-2206 while the other one-half received 75 to 100 mg. of demerol (17 cases) and $\frac{1}{32}$ grain of dilaudid (12 cases). In 10 other cases where two-stage thoracoplastics were performed an excellent opportunity prevailed to compare Nu-2206 to other drugs. Thus, 5 of these received Nu-2206 following the first-stage thoracoplasty and one or the other drug following the second stage. The other 5 patients received demerol or dilaudid following the first stage, and Nu-2206 following the second stage.

TABLE I

NUMBER OF CASES	NU-2206	DEMEROL	DILAUDID	TOTAL ADMINISTRATIONS
57 Single-stage procedures	28	17	12	57
10 Two-stage thoracoplasties				
1st stage	5	3	2	10
2nd stage	5	2	3	10
Total 67	38	22	17	77

Demerol was disappointing. It proved quite ineffective in overcoming postoperative pain. From Fig. 2 one can anticipate minimal to moderate pain relief for 2 to 3 hours in the majority of instances. Only rarely will the drug be effective for as long as 5 hours. As a rule the patients cough, breathe deeply, and expectorate ineffectively and with marked difficulty. Their movements from side to side are guarded and performed with considerable misgiving. Nurses devote considerable time to these patients, prodding them through their routine exercises. Some typical responses from many patients were: "No relief from hypo," "not much relief," "can't move because wound will break open," "poor pain relief." The nurses objected not only because of the considerable time element involved in stir-up exercises, but also because their persuasion methods appeared cruel. Statements taken from nurses' notes were: "Coughing and deep breathing must be forced," "patient uncooperative for stir-up regimen," "cannot or will not cooperate in turning or expectorating," "uncooperative in turning, deep breathing, coughing and forceful persuasion is necessary." Only once was a good report found: "Cooperative; good pain relief throughout administration."

Except for 1 case of atelectasis, no other noteworthy complication was noted. Confusion was seen for 36 hours in 1, and nausea and vomiting within the first 48 hours postoperatively in 4 patients.

In general, dilaudid was superior to demerol, producing moderate to complete analgesia for 3 to 3½ hours (Fig. 3). During the period of analgesia the patient's apprehension disappeared and was replaced by a feeling of relaxation, which rarely occurred with demerol. Furthermore, the routine stir-up exercises were accomplished with relative ease. In the 12 patients studied, the only complication noted was nausea and vomiting for 48 hours postoperatively in 1 patient.

Nu-2206 proved to be an extremely effective analgesic with a longer period of action. Average analgesia was for 7 hours, representing approximately twice the duration of dilaudid and three times that of demerol (Fig. 4). As a rule, pain relief was complete and patients cooperated readily in undertaking their exercises. Patients with previous experiences in other pain relieving drugs following chest surgery emphasized this drug gave faster, longer, and more complete relief than any other they had received. Actually, if the duration and extent of analgesia provided by demerol and Nu-2206 were plotted, the resulting rise of the curves would be at opposite ends. In demerol the height of the curve is early and drops immediately, whereas in Nu-2206 the curve is highest at a late period. The curve produced by dilaudid would be between the two.

dramatic that the patients felt the drug had curative powers. This feeling of well-being or euphoria was observed in all but 2 cases. This euphoria was unlike that seen with morphine, for these patients had excellent judgment and good insight.

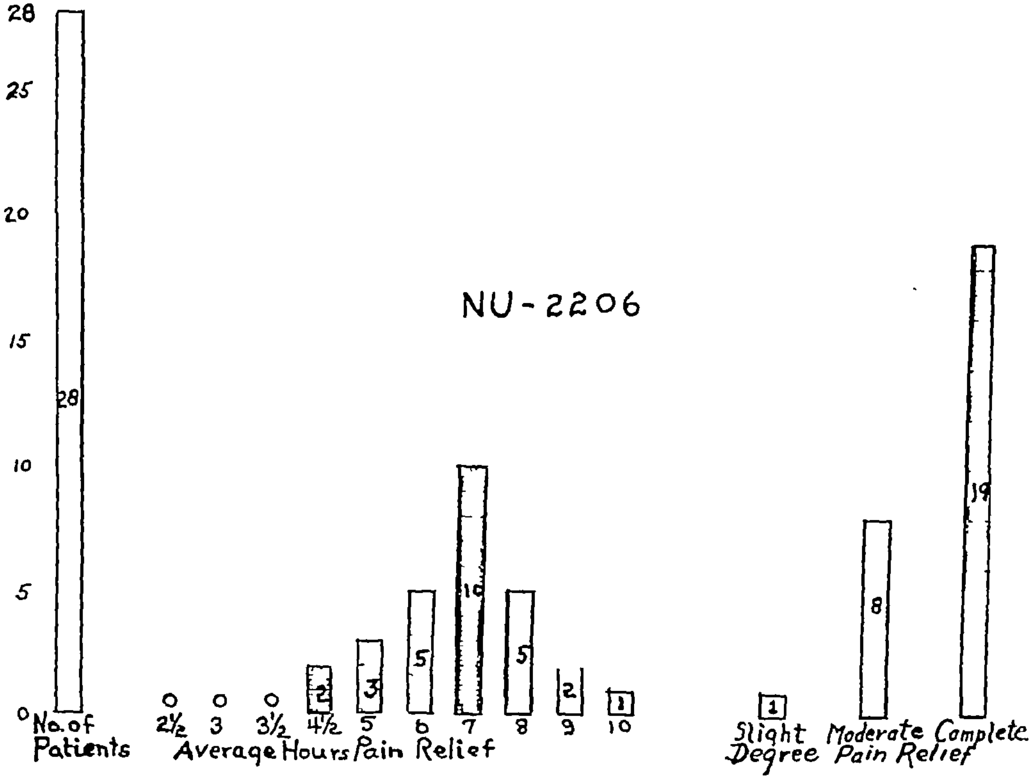

Fig. 4.—Demonstrates long action of Nu-2206.

Another case, which was not included in this series because it was not within the scope of this study, is cited because of its interest and value. A 55-year-old dentist, a brother of a physician, suffering from malignant hypertension, encephalopathy, and chronic passive congestion of the lungs, complained of dyspnea, apprehension, and extreme nervousness. A trial of demerol and practically all barbiturates produced either marked excitement or depression. He had not slept for 8 days when his brother suggested a trial of Nu-2206. The physician was cognizant of the fact that since no pain was present a respiratory depression might ensue. For the first time in 2 months the patient slept 8 hours. Following the injection of another 5 mg. the next morning the relief was so great that he was certain the vicious spasm was broken and a cure might result. Nu-2206 continued to relieve him for 8 to 10 hours until he died 2 weeks later.

A word of caution must be interjected at this point. This drug has an action similar to other narcotics, producing respiratory depression if no pain is present. The following case exemplifies this situation. A highly excited patient without pain was given 5 mg. of Nu-2206 and the respiratory rate promptly dropped to 8 per minute for a 4-hour period. Had comparable doses of morphine or dilaudid been given, we believe a similar picture might have occurred.

Complications observed with the use of Nu-2206 in 28 patients were as follows: One patient was confused, lethargic, nauseated, and vomited for the first 36 hours. Two patients had nausea and vomiting which could be attributed to the drug, and 1 had a drop in respiratory rate to 14 per minute. At no time did such disturbing untoward effects as leucopenia, sensitivity reactions, or shock develop. Four patients received Nu-2206 from 4 to 8 weeks, and in only 1 instance was increasing tolerance to the drug entertained but not proved. In this same group 1 died from malignancy, while the other 3 developed neither withdrawal symptoms nor a desire for its continued use after the drug was stopped.

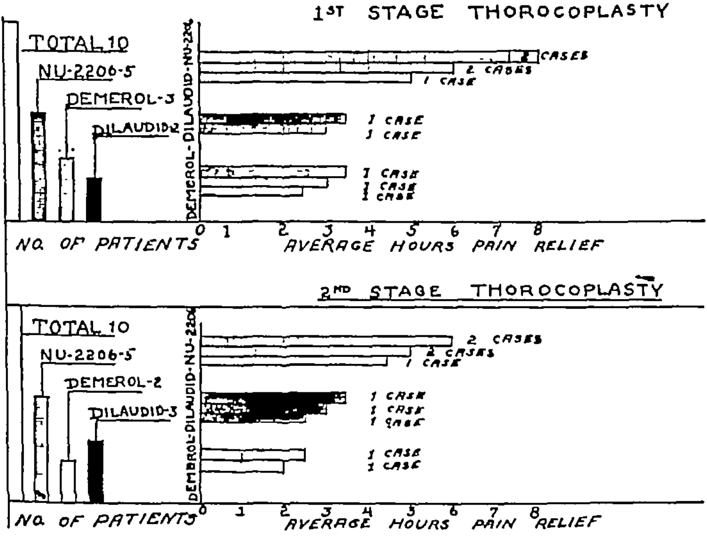

Fig. 5.—Comparison of Nu-2206 with demerol and dilaudid in first- and second-stage thoracoplastics.

The advantage of Nu-2206 over demerol and dilaudid was, in our opinion, definitely shown in instances where two-stage thoracoplasties were performed. Those receiving Nu-2206 following first-stage thoracoplasty received average pain relief for 6 to 8 hours, while demerol and dilaudid aided for 2½ to 3½ hours. Following the second-stage thoracoplasty, at which time the pain is more intense and more difficult to control, demerol at best only partially controlled the pain for to 2 to 2½ hours. Dilaudid was somewhat better, producing moderate to complete relief for 3 to 3½ hours, and Nu-2206 gave practically complete relief from 5 to 7 hours (Fig. 5).

SUMMARY

1. While the number of cases studied is small, the results definitely demonstrate the superiority of Nu-2206 over demerol and dilaudid.

? Demerol should not be employed alone for pain relief in thoracic lesions. Its action is short and the extent of relief is minimal. Preferably it should be combined with some other agent, such as codeine.

3. Dilaudid proved quite efficacious for short periods of time.

4. Nu-2206 offered pain relief for a longer period of time, averaging twice and three times as long as dilaudid and demerol, respectively.

5. The extent of pain relief from Nu-2206 was moderate to complete in this series.

6. The effective and prolonged action of Nu-2206 provides the nursing staff with more time for other necessary duties. It makes unnecessary the highly undesirable, forceful persuasion so frequently required with other analgesics for stir-up exercises.

7. It has been shown elsewhere that because it has a wide margin of safety Nu-2206 is a safe drug to use clinically.

8. This small series demonstrated no unusual side effects and the incidence of nausea and vomiting was no greater than with demerol or dilaudid.

9. In the presence of pain the administration of Nu-2206 will not produce respiratory depression.

10. The small number of cases in which this drug was used over a prolonged period preclude a definite statement regarding the development of tolerance. However, the drug was used successfully in patients developing a tolerance and addiction to morphine. These patients did not develop withdrawal symptoms nor show a desire for continued use of Nu-2206 when the drug was stopped.

11. For many of the preceding reasons this drug is desirable for minimizing pain in inoperable carcinomas.

12. In our opinion, Nu-2206 has a real place in the control of pain due to thoracic lesion.

Note.—We have just been notified that the Bureau of Narcotics of the Department of the Treasury has reported that Dromoran is to be labelled as an addiction-forming or an addiction-sustaining liability drug similar to morphine and as an opiate. We have no reason to challenge this decision. It will probably become effective on or about Feb. 20, 1950. This means, consequently, that all clinicians and others who are requesting Dromoran from us must be asked to order their supplies after February 20, accompanied with the usual Federal Order Form for Narcotics.—*Hoffmann-La Roche, Inc.*

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PULMONARY HISTOPLASMOSIS: REVIEW OF PUBLISHED CASES AND REPORT OF AN UNUSUAL CASE

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IN RECENT years histoplasmosis has been much discussed particularly by physicians interested in thoracic diseases. Yet, the number of proved cases remains small and knowledge concerning this disease is limited.

In March, 1948, we saw a patient whose illness we thought to be due to an infected pulmonary cyst. Right lower lobectomy was performed, and the pathologist made the diagnosis of histoplasmosis which was subsequently confirmed by culture. We were somewhat surprised as the patient presented none of the clinical characteristics commonly attributed to this disease. Therefore, we undertook to review all the published cases of histoplasmosis in order to assimilate available information with particular reference to the pulmonary aspects of the disease. It is this information as well as a report of our case that we are presenting herein.

We were able to find 123 cases of histoplasmosis recorded in the literature up to 1949. In 62 of these we considered pulmonary involvement proved. This article will deal primarily with these 62 cases but first of all a few comments on the entire group of 123 cases seem desirable.

We found that the age of the patients ranged from 7½ weeks to 77 years and, interestingly enough, about one-sixth of them were less than 1 year of age. Male patients outnumbered the female by more than 2:1. These patients lived in twenty-five different states of the union and seventeen foreign countries embracing much of the world but, unquestionably owing to more intense interest here than elsewhere, the United States accounted for more than three-fourths of them.

Nearly two-thirds of these patients had significant anemia and a like number leucopenia. Cultures to recover the organism seemed to have a high degree of reliability. In 60 cases one or more cultures were made, and *Histoplasma capsulatum* was recovered from at least one culture in 53 of them. Material from 16 patients was inoculated into animals. In only 8 of these was the organism recovered.

One-half of the 24 patients who were tested with histoplasmin were found to be nonreactors. When we considered this high percentage of nonreactors among those who have the disease, plus the fact that a large number of the normal population are positive reactors we concluded that the test in its present form is without value to the clinician. It may, however, be of importance to the epidemiologist. The complement fixation and precipitin reactions are unreliable procedures because of cross reactions with other organisms.

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No satisfactory treatment for histoplasmosis has yet been found although many different medicaments have been given a trial.

PATHOLOGIC ASPECTS

In 90 of the 123 cases necropsy was conducted. From observations in these 90 cases it is known that the most frequently involved organs in order of frequency are the lymph nodes, liver, lungs, spleen, adrenal glands, intestines, bone marrow, kidneys, and oropharynx.

Histoplasmosis of the lungs does not have any specific histopathologic features. In the lungs the lesions are usually curious mixtures of necrosis, exudation, and proliferation. The necrotic material seldom liquefies but liquefaction has been found to occur in a few instances. The exudate usually is composed of polymorphonuclear cells and lymphocytes. The proliferation is usually a mixture of fibroblasts and tissue macrophages. The latter are likely to contain the organisms englobed in the cytoplasm. In such cases the appearance is fairly characteristic and may be the clue to the diagnosis. In some instances the diagnosis has been confused with toxoplasmosis, leishmaniasis, and cryptococcosis. In some cases the organisms may not be demonstrable in histologic sections but may be demonstrated only by culture. There is evidence that the lesions tend to become calcified within a few months if healing occurs. The lesions may be single or multiple. In the lung they may be in any portion and the regional lymph nodes may or may not be involved. If the lesion is near the periphery of the lung there may be pleural effusion. Thus, the pulmonary lesions may give clinical manifestations closely simulating those of tuberculosis.

The lesions in other viscera do not differ fundamentally from those found in the lungs. From the reported cases it is evident that histoplasmosis may involve any organ or tissue either individually or collectively. In some cases only one organ is involved, and the condition is discovered incidentally at necropsy, while in other cases there is extensive involvement of every organ and tissue of the body. Histoplasmosis was found to be associated with tuberculosis in 13 of the 123 reported cases, with Addison's disease in 6, Hodgkin's disease or lymphoblastoma in 4, diabetes mellitus and syphilis in 3 cases each, and leucemia in 2. The amount of necrosis varied. Liquefaction is not the rule but may occasionally occur, especially in the adrenal glands and in the periarticular, submucosal, and subcutaneous tissues. The lymph nodes and spleen may or may not be involved. If a local lesion is near the surface, either of the skin or mucous membrane, it is likely to ulcerate and the ulcer tends to become chronic. In a recently developed lesion the organisms are usually present in large numbers and can be demonstrated by histologic examination of specimens. In older lesions the organisms may not be demonstrable in histologic preparations so cultures may be necessary to prove their presence. In ulcerative lesions the histologic pattern may be altered according to the degree and kind of secondary infection. The ulcerative lesions have no gross diagnostic characteristics and have been found to occur on the neck, face, hands, vulva, anus, penis, lips, buccal mucosa, alveolar ridge, tongue, palate, pharynx, larynx, esophagus, and intestine.

PULMONARY LESIONS

From this point on our discussion will be limited to the 62 cases in which we considered pulmonary involvement by *H. capsulatum* definitely proved. In order to avoid any erroneous assumptions, only those cases were accepted for this group in which involvement of the lung was proved by one of the following means: visualization of the organisms in histopathologic sections of the lung, bronchi, or peribronchial lymph nodes; culture of the organisms from pleural fluid; culture of the organisms from sputum or gastric material if no oropharyngeal lesions were present from which the organisms may have come. Undoubtedly a number of cases of pulmonary involvement were excluded by adherence to these restrictions.

Of the 62 patients, 41 were males and 19 females and for 2 the sex was not reported. The age of these patients varied from 7½ weeks to 72 years. Fifteen were less than 1 year of age.

A list of symptoms associated with pulmonary lesions in these cases is recorded in Table I. Cough was the most common respiratory symptom and was recorded in 27 of the 62 cases. Physical examination of the chest demonstrated findings to correspond with the various underlying lesions, but in many cases nothing abnormal was noted.

TABLE I. SYMPTOMS ASSOCIATED WITH PULMONARY LESIONS IN SIXTY-TWO CASES OF HISTOPLASMOSIS

	CASES		CASES
Fever	52	Sweats	13
Loss of weight	29	Pain in chest	9
Cough	27	Expectoration	6
Weakness	18	Hoarseness	6
Dyspnea	15	Hemoptysis	5
Chills	13	Cyanosis	3

Roentgenograms of the thorax were made of 45 of these 62 patients, and for 8 they were reported as negative for disease. Of the 37 patients whose roentgenograms revealed positive evidence of disease, 30 of them had bilateral disease. Twenty of these 30 had widespread involvement of all regions in both lungs. Any attempt to correlate the written description of pulmonary lesions as given by various roentgenologists is hazardous at best, but we can interpret their statements well enough to classify the findings rather roughly. Some patients had lesions of more than one description, therefore, the number of cases does not check correctly with the total number. In the largest group, 17 cases in number, the roentgenograms were described variously as indicating "bronchitis," or "peribronchial infiltration," or merely as showing "increased bronchovascular markings." In another group of 16 cases they were described as showing localized areas of infiltration or bronchopneumonia. In 5 cases they showed evidence of pneumonic consolidation or the "pneumonitis" type of picture. In 3, generalized miliary involvement was the roentgenologic diagnosis. In 3 others there was evidence of definite nodules, either discrete or conglomerate. In only 4 cases were the lesions distributed so that they resembled the reinfection type of tuberculosis in the apical regions. To summarize then, we can say that there is no characteristic roentgenographic pattern for histoplasmosis of the lungs. The lesion seldom shows cavitation, may be associated with calcification, infrequently resembles tuberculosis, and in only about one-third of the cases does it have the pattern which is ordinarily considered characteristic of fungus infections, that is, peribronchial infiltration extending radially outward from the hilar region. Further data on this statement concerning calcification and cavitation will be considered next.

Although necrosis of pulmonary lesions is common, cavitation seems to be unusual. We could find only 3 cases in which cavities were found and in only 1 of these was the cavity definitely proved to be caused by *H. capsulatum.*[1] In 1 case[2] the cavity was probably due to tuberculosis, and the third patient[3] is still living and therefore, the cause of cavitation remains unproved. Calcification was associated with pulmonary histoplasmosis in 8 of these 62 cases. Much interest has been aroused in the work of recent years which shows a high degree of correlation between pulmonary calcification and positive results from skin tests with histoplasmin on persons who have negative reactions to tuberculin. This work gives strong circumstantial evidence that histoplasmosis does cause pulmonary calcification, but only recently has the absolute proof been established. Christie and Peterson[4] found calcifying hilar and parenchymal lesions during necropsy and obtained *H. capsulatum* from these lesions on culture. Thus, they proved for the first time what had been thought to be true for several years. Bunnell and Furcolow[5] previously presented rather convincing evidence of the same circumstance in one of their case reports.

In cases of pulmonary histoplasmosis, cultures of sputum, pleural fluid, and gastric material should give a high percentage of positive results. Unfortunately, this was attempted in only a very few of these cases. However, the diagnosis was established by positive culture of gastric material in the case of 2 patients, and of sputum in 2 others.

It is interesting that the diagnosis was definitely established before death in 23 of the 62 cases of pulmonary histoplasmosis. Five of these patients were still living at the time their cases were reported. The longest survival time reported after diagnosis was two years, and the patient was still living at the time of the report.

REPORT OF CASE

The patient, a man 36 years old, who lived near the Mississippi River in Iowa, was admitted to the Mayo Clinic March 3, 1948. His wife and three children were living and well. Medical history was not significant except that in 1937, a roentgenogram of the thorax was taken in the course of an employment examination and he was told that he had two lesions in the lower part of the right lung. This was again noted in 1942, when he was rejected by the draft board because of the pulmonary lesion.

The patient remained asymptomatic, however, until Dec. 24, 1947, when he expectorated blood, about 4 or 5 tablespoonfuls (60 to 75 c.c.). Although he felt well, he consulted his physician who took a roentgenogram of the thorax and noted a mass the size of a grapefruit in the lower part of the right lung. Sputum was said to contain pneumococci, and penicillin and streptomycin were prescribed. On Jan. 9, 1948, bronchoscopic examination was performed and foul-smelling coffee-colored pus was aspirated from an indurated right lower lobe bronchus. After this procedure the patient coughed up approximately 1 cupful of sputum per twenty-four hours. Bronchoscopic examination was repeated Jan. 10 and Jan. 30, 1948. Radiopaque oil was instilled into the bronchi at the time of bronchoscopic examination on January 30. Following this third bronchoscopic examination the patient raised a large amount of pus and coffee-colored material, estimated by the patient to be about 1 quart (1,000 c.c.). After a fourth bronchoscopic examination on Feb. 18, 1948, the color of the sputum changed to pink. During this time the patient's general condition remained good and he had a good appetite. Temperature usually rose each day to a maximum of 99° to 100° F. He lost between five and ten pounds (2.3 to 4.5 kilograms). Two days before admission to the clinic rather sharp shooting pains developed through the right lower part of the thorax. Before admission to the clinic he had been given penicillin and streptomycin on several occasions but the amount and duration of this treatment we do not know. It had no apparent effect on the illness.

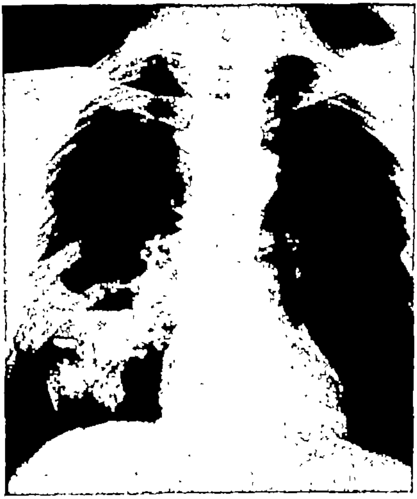

Fig. 1.—The thorax on March 4, 1948, before operation.

At the time of admission to the clinic, March 3, 1948, the patient appeared well in spite of the rather prolonged illness. On examination the blood pressure was found to be 114 mm. of mercury systolic and 60 diastolic. The pulse rate was 76 beats per minute, and temperature was 99° F. Numerous râles were heard over the right lower portion of the thorax posteriorly, but the examination otherwise gave negative results. No hepatosplenomegaly was present.

Laboratory studies were reported as follows: The urine was normal. The concentration of hemoglobin was 12.8 Gm. The erythrocyte count was 4,610,000 per c.mm. of blood. The leucocyte count was 7,700 of which 10 per cent were lymphocytes, 11 per cent monocytes, and 79 per cent neutrophils. The sedimentation rate was 42 mm. in one hour by the Westergren method. Flocculation test for syphilis gave negative results. No acid-fast bacilli were seen on direct examination of the sputum but gram-positive cocci and an organism which was suspected of being *Candida albicans* were noted. The sputum was cultured for tuberculosis and the culture was subsequently reported to be negative for these organisms. Cultures of the sputum for fungi also were inoculated on culture media at the time of admission and were later reported to be positive for *H. capsulatum* but this report was not available until several days after operation. Roentgenograms of the thorax (Fig. 1) showed a large thick-walled cystic lesion with a fluid level in the upper portion of the right lower lobe. Roentgenograms made with the patient lying down on his side demonstrated free fluid in the cavity. There was also an irregular collection of radiopaque oil in the right lower lobe. The roentgenologist interpreted these findings as probably representative of an infected pulmonary cyst.

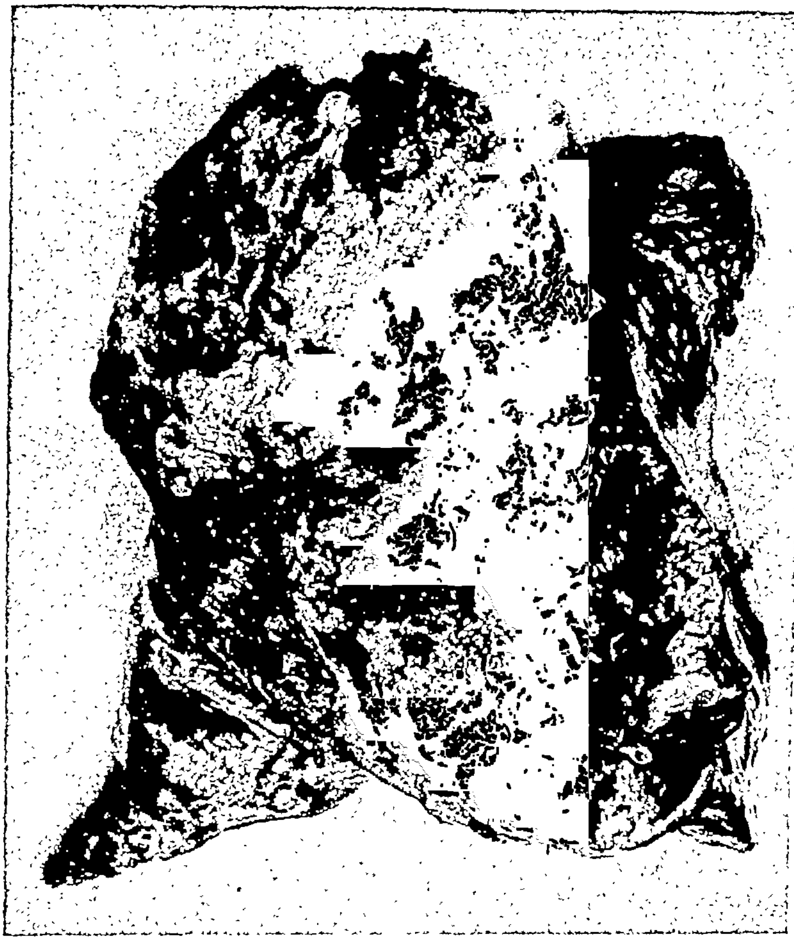

Fig. 2.—The cut surface of the mass removed. The grayish white area in the upper portion was dry and crumbly. The cut portions of the multilocular cavity should be noted also. A small isolated subpleural nodule of histoplasmosis is shown in the lower left portion of the photograph.

A preoperative diagnosis of infected cyst of the lung was made. On March 6, 1948, three days after admission, a right lower lobectomy was performed by one of us (O. T. C.). The pathologist* made the diagnosis of histoplasmosis. The lesion was a firm, almost spherical, grayish white mass measuring 9 by 7 by 4 cm. (Fig. 2). In cross section it appeared to have a fungating center suggesting that there had been enough necrosis to give the semblance of a cavity. The cut surface was dry, crumbly, grayish white with streaks of lighter gray tissue indicative of extensive fibrosis. Contained within the larger mass was a second smaller mass of similar color and consistency but sharply outlined by a dense grayish white band of firm tissue. In addition, in the adjacent parenchyma of the lung, there were three smaller, grayish white, sharply circumscribed nodules 2 to 3 cm. in diameter with crumbly necrotic centers resembling old abscesses. Cultures and smears from each of these lesions revealed *H. capsulatum* (Fig. 3). No other organism was found on culture or animal inoculation.

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*Dr. J. R. McDonald.

Histologic sections of the granulomatous masses showed varying degrees of necrosis and fibrosis with infiltration of lymphocytes, plasma cells, and various tissue phagocytes containing *H. capsulatum*. One interesting feature was the presence of the organisms within the cytoplasm of the fibroblasts. Attention has previously been called to the presence of the organism in cells of the adrenal cortex and liver cells. The presence of the organisms in tissue cells suggests the possibility of an invasive capacity on the part of the organism rather than a phagocytic capacity on the part of the cells. Cultures of the sputum after operation failed to reveal the organisms, and cultures of the blood and urine also were negative for this organism.

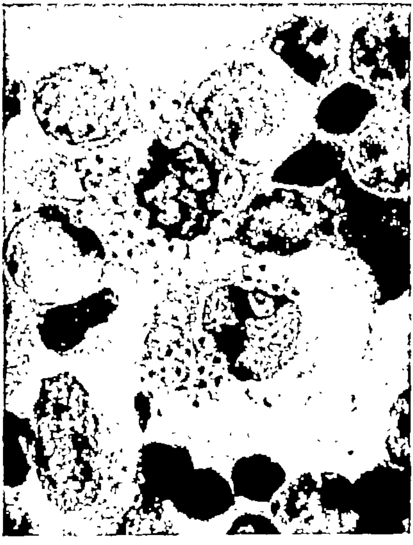

Fig. 3.—*Histoplasma capsulatum* in phagocytes. Wright stain of an impression smear from the cut surface of the lesion shown in Fig. 2 (× 1,500).

Skin tests were performed in the postoperative period with the following results: 0.0001 mg. of tuberculin (P. P. D.) gave a positive reaction of 2+; coccidioidin and Blastomyces vaccine gave negative results and histoplasmin a doubtfully positive result.

The patient was up on the fourth day after operation and left the hospital on the tenth day. He was last heard from in March, 1950, two years after operation, at which time he was examined by his local physician who reported that the patient had no symptoms, was working eight hours a day as a carpenter, and a roentgenogram of the chest revealed that both lungs were entirely clear.

It would not be wise to predict the ultimate outcome for this particular patient. It is well known that histoplasmosis may be present for years without serious consequences and yet ultimately prove fatal. Perhaps some latent focus may come to light in the future. On the other hand there is good reason to believe that some patients do recover completely from this infection and as our knowledge of the disease expands we can expect to see more who go on to recovery.

In considering this case in retrospect we have asked ourselves whether we would have recommended exploration of the thorax if we had known that this patient suffered from histoplasmosis. Perhaps we would not, but at least in this particular case this treatment seems to have been satisfactory. However, the nature of the disease and its tendency to disseminate would suggest that the disease in only the rarest of cases will be amenable to any form of surgical treatment. In the literature we found a report of only I case of histoplasmosis in which pulmonary resection was carried out.[6] In that case, lobectomy was performed because of massive pulmonary hemorrhage. *H. capsulatum* was not found in the lobe removed either by microscopic study of the tissue or by culture even though the patient had proved histoplasmosis elsewhere in the body.

ADDENDUM

Since submitting this article we have performed lobectomy for histoplasmosis on an additional patient, a woman from Illinois who was 35 years old. The only evidence of disease was found in the right upper lobe of the lung. Sputum cultures had been reported positive for *Histoplasma capsulatum* before the patient came to the Mayo Clinic and this finding was confirmed at the clinic. Right upper lobectomy was performed on Nov. 15, 1949. The pathologist reported chronic granuloma with cavitation but no organisms were seen in the histologic sections. Cultures of the specimen were positive for *H. capsulatum.* The patient was living and well in mid-March, 1950, four months after lobectomy. A roentgenogram of the thorax at that time showed no evidence of a pulmonary lesion.

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PARTIAL PERICARDIECTOMY IN A CASE OF HEMOPERICARDIUM DUE TO NONPENETRATING TRAUMA

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THE occurrence of hemopericardium due to nonpenetrating trauma is a rare condition, and a search of the literature fails to reveal a single instance in which pericardiectomy has been employed as a primary surgical therapeutic measure.[1] In a comprehensive discussion of the etiology of acute hemopericardium, Fulton[2] listed trauma of the penetrating variety as one of the most frequent causes but did not specify nonpenetrating injuries as an etiological factor. In 1940, Warburg[3] at Copenhagen collected from the world literature a total of 261 cases of myocardial or pericardial damage due to nonpenetrating blunt injuries. In at least sixty cases there was pericardial involvement with either effusion or hemorrhage. He noted that pericardiocentesis was rarely necessary and cited only one case (Moullen, 1897) in which a large amount of fluid was removed by pericardiotomy.

CASE REPORT

The case which is to be reported here is that of a 29-year-old businessman, S.S., who was admitted to Doctors Hospital on March 11, 1948, for further evaluation of a proved pericardial effusion. The diagnosis had been established three months previously at the Jewish Memorial Hospital. He was first admitted to the latter hospital on Dec. 5, 1947, with a two weeks' history of dyspnea and chest pain, both aggravated by exertion; he also complained of a severe nonproductive cough. In the five days preceding admission the symptoms became intensified. Two months prior to admission he had experienced a sudden tearing pain across the chest following a kick on the chest by his 3-year-old daughter with whom he was playing. One month before admission he claimed that his chest had been compressed by a large packing case which he was lifting. Another instance of trauma to the chest had occurred in the more remote past—two years prior to admission he had struck his chest against the steering wheel in an automobile accident. Otherwise the past history was noncontributory.

Notable findings on physical examination at the Jewish Memorial Hospital were dyspnea and cyanosis, marked distention of neck veins, and an enlarged heart. The heart sounds were distant. The blood pressure in the right arm was 135/110, in the left arm 115/85. There was slight dullness in the left chest posteriorly. The liver was palpable 3 c.m. below the costal margin; it was regular in contour and slightly tender.

The x-ray examination showed a cardiac outline (Fig. 1) which was enlarged in all diameters, the silhouette being of the "dewdrop" type. The electrocardiogram revealed low voltage of the QRS complexes and inversion of T_1, T_2, and T_4. The venous pressure was 290 mm. of saline on admission. Following a pericardial tap of 400 c.c. of blood on Dec. 13, 1947, there was gradual clinical improvement with a fall in venous pressure to 122 mm. of saline on discharge. One month later the patient was admitted overnight for a second pericardial aspiration; again 400 c.c. of bloody fluid was removed. Cytologic studies were done; only blood and fibrin were visible, with no tumor cells evident. Studies for organisms, including acid-fast bacilli, were negative. No evidence of pericardial tumor was demonstrated when air was injected into the pericardial sac. To rule out the presence of a neoplastic process pericardiotomy was advised.

Upon admission to Doctors Hospital the same symptoms were present, although they were of a lesser degree. On physical examination there was no longer any venous engorgement in the neck. The lungs were clear and the cardiac findings were unchanged. The liver was not palpable. The roentgenographic picture was relatively unchanged, as was the electrocardiogram. The venous pressure was 130 mm. of saline.

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Laboratory studies showed a hemoglobin of 11.5 Gm. Red blood cells were 4.28 million. White blood cells were 10,700 with a normal differential. Urinalysis was negative. The blood sugar was 162 mg. per cent. After consultation an exploratory pericardiotomy was advised to determine the cause of the persistent bleeding within the pericardial sac.

On March 16, 1948, under endotracheal anesthesia, a horseshoe-shaped incision was made on the left anterior chest wall with the horizontal limbs over the third and sixth ribs, the verticle limb overlying the midsternum. After the skin and pectoral muscles were elevated laterally, the fourth and fifth costal cartilages with 2.5 cm. of the adjoining ribs were resected. The internal mammary vessels were ligated, and the flap of intercostal muscles was elevated and displaced laterally exposing the pericardium and pleural reflection.

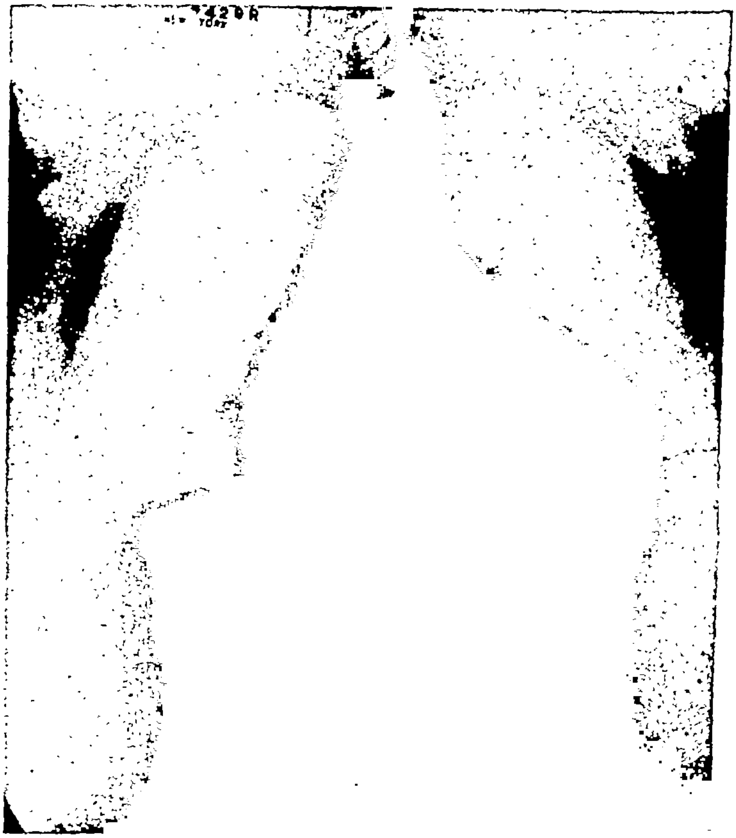

Fig. 1.—Anteroposterior view of chest showing enlarged cardiac shadow due to pericardial exudate.

The parietal pericardium was bulging and definitely thickened; the visceral pericardium and the internal surface of the parietal pericardium were finely granulated and bled freely on contact. About 400 c.c. of dark liquid blood was removed. On thorough inspection of the heart no abnormalities were found. The great vessels appeared normal. The coronaries could not be visualized because of a thin deposit of fibrin over the visceral pericardium which also appeared to be slightly thickened, but on palpation the blood flow seemed normal. Several large plaques of fibrin were removed from the pericardial sac which was then irrigated with isotonic saline solution. All adhesions between the visceral and parietal pericardium were divided. In order to avoid further bleeding from contact of visceral and parietal pericardium, to promote drainage, and to eliminate the possibility of later constrictive pericarditis, a resection of the pericardium was decided upon. Approximately two-thirds of the anterior pericardium, especially that portion overlying the ventricles, was then resected. The cut margins were sutured with 0 plain catgut to control oozing. The muscular flaps were then sutured back in place, and the skin edges approximated with silk sutures.

The pathologic specimen removed at operation consisted of two strips of parietal pericardium measuring 5.1 by 2.4 by 0.5 cm. and 6.4 by 2.7 by 0.6 cm. The outer surface was gray and gelatinous while the inner lining was dark red and hemorrhagic.

The pathologist described the following microscopic findings: The inner region consisted of edematous granulation tissue and recent hemorrhage. On the surface scattered patches showed organization of fibrinoid substance. The outer region revealed compressed fibrous tissue throughout which were many nutrient vessels surrounded by cuffs of lymphocytes.

A concentrated specimen of the pericardial fluid was examined by direct smear and was found to contain no acid-fast bacilli. A Petragnani culture of the fluid was negative after two months.

Fig. 2.—Anteroposterior view of chest following pericardiectomy. Structure within normal limits.

The pathologic diagnosis was chronic fibrous pericarditis with old and recent hemorrhage.

For a week following operation the patient ran a febrile course which was not altered by antibiotics. On March 23, 1948, temperature had fallen to 99° F. and from this point on he remained afebrile. An electrocardiogram taken on the day after operation showed that, although they were still present, the ST- and T-wave changes were less marked.

This patient was discharged on the tenth postoperative day. Aspiration of a hematoma was required twice following discharge from the hospital. Examination six months after operation showed the blood pressure and venous pressure to be normal, and the patient free of complaints. Roentgen examination of the heart showed a normal heart outline (Fig. 2). There have been no signs of cardiac failure.

COMMENT

If pericardiectomy with thorough exploration of the pericardial sac had not been done, it might be argued that traumatic etiology of the hemopericardium was probable but that a neoplastic process would have to be eliminated. With exploration the possibility of tumor, either primary in the pericardium or invasive from an adjacent structure, has been ruled out. The great vessels at the base of the heart were found to be grossly normal.

A generous biopsy specimen was obtained, permitting microscopic study of the pathologic changes which have been described. No evidence of periarteritis nodosa or other diffuse vascular disease was apparent in the specimen. No single bleeding point was found; rather, a diffuse edematous granulation tissue with recent hemorrhage was the most striking finding. Doubtless, there was considerable oozing of blood from this surface. The possibility of bleeding from this source initially is improbable if the original lesion was traumatic in origin.

Similar granulomatous changes in the epicardium were described in a case report which appeared in the Swiss literature in 1941.[4] This patient, a 66-year-old woman, suffered from longstanding cardiac insufficiency and, at postmortem examination, was found to have a rheumatic endocarditis with severe mitral stenosis. In addition, she had a massive hemopericardium with telangiectatic granulomatous changes with multiple hemorrhage in the epicardium. However, a rather unusual additional finding was the presence around the blood vessels of numerous collections of cholesterol crystals surrounded by giant cells. There was no history of trauma in this case.

Trauma, in the case under discussion, seemed to be the most significant etiological factor with neoplasm and blood vessel disease eliminated. There was no reason to suspect that the patient had a blood dyscrasia or a bleeding tendency of any sort. Since three different instances of trauma were elicited in the history, appraisal of these injuries is necessary. Of the three injuries sustained (Injury A: kick in the chest; Injury B: pressure from packing case; Injury C: striking chest against steering wheel), only injury A was recalled by the patient at the initial interview, injuries B and C being remembered only when prompted by the historian. It seems rather improbable that injury C, which had been sustained two years before admission, could be responsible for an alteration in circulatory dynamics which appeared only two weeks before admission. Injury B was not accompanied by pain in any way approaching the magnitude of the "sudden, tearing pain" experienced in injury A. Apparently injury A was by far the most severe traumatic event experienced by the patient. It is possible that the other injuries in some way may have contributed to the trauma sustained.

SUMMARY

1. A case of hemopericardium, believed to be the result of nonpenetrating trauma, is presented.

2. A partial pericardiectomy was performed and the pathologic findings are discussed.

3. To the best of our knowledge, pericardiectomy has never before been attempted in this condition.

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PULMONARY PROSTHESIS AFTER PNEUMONECTOMY

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THE history of Lucite (methyl methacrylate) used experimentally and in clinical surgery has been excellently reviewed and brought up to date by Wilson. He made experimental studies and demonstrated a clinical use for Lucite balls in the plombage operation in the surgical treatment of pulmonary tuberculosis.[1, 2, 3] Pulmonary prosthesis was developed by Johnson and associates.[4, 5] These authors have presented the work so well that it would be useless to review it. Harrington[6] stated that Claggett wished to avoid thoracoplasty after pneumonectomy and used pulmonary prosthesis. In order to prevent overdistention of the remaining lung after pneumonectomy Cournand and Berry[7] used oil with good results. The necessity for and the justification of pulmonary prosthesis depends upon two somewhat controversial theories: (1) overdistention of the remaining lung after pneumonectomy results in an impairment of the cardiorespiratory function, and (2) overdistention of the remaining lung after pneumonectomy for pulmonary tuberculosis enhances the activation or flare-up of dormant or quiescent tuberculous lesions in the remaining lung. *Thoracoplasty prevents overdistention and is not a prosthesis but it does obliterate the empty pleural space. It has an advantage over prosthesis* since it will prevent or heal empyema. If empyema complicates the pneumonectomy a prosthesis is contraindicated and thoracoplasty is imperative. Thoracoplasty is deforming.

Whether cardiorespiratory impairment develops seems to involve several considerations. Does hyperplasia of the remaining lung tissue occur; is compensatory hypertrophy of the lung developed, or does emphysema of the remaining lung occur? The age of the patient and the patient's predestined future concerning the development of emphysema or cardiac failure, even with both lungs intact, are important factors in answering these questions.

Hyperplasia of lung tissue in young animals after pneumonectomy has been demonstrated by Haasler (1892),[8] Mollgaard and Rovsing (1910),[9] Kawamura (1914),[10] Knott (1934),[11] Hilber (1934),[12] Bremer (1937),[13] and Longacre and associates (1940).[14, 15, 16] There is no dissenting opinion. It has not been proved, however, whether hyperplasia will occur in the remaining lung after pneumonectomy in babies or children.

In 1935, Rienhoff[17] reported that experimental studies and the study of agenesis[18] of the lung indicated that compensatory dilatation and not emphysema of the lung occurs after pneumonectomy. The conclusion is based upon the study of the lung from one adult dog about six months after pneumonectomy. At a meeting in 1948, Rienhoff[19] referred to this work, stressing the point that

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emphysema does not occur in the remaining lung after pneumonectomy. Smart[20] in a study of agenesis of the lung collected 104 cases from medical literature and added two more patients that he had studied. Fifty-seven autopsies were performed, but the existing lung was described only seven times and in six there was emphysema. Longacre[14, 15, 16] made exhaustive experimental studies on dogs after pneumonectomy. He carried out this procedure on puppies and studied the results on three such dogs two, three, and almost four years later. From the same litter he kept two puppies as controls. He did pneumonectomies on young adult dogs and studied the results on two of these animals two and almost four years afterward. Histologically the lungs from the dogs which had pneumonectomies as puppies were larger than normal with smaller than normal alveoli; however, the atria were dilated and suggested hyperplasia. A histologic study of the lung from the dogs that had pneumonectomies when young adults showed no hyperplasia but dilatation and definite emphysema. Longacre's conclusions and results differed from those of Rienhoff on young adult animals. Rienhoff studied the lung of his dog six months after pneumonectomy. Longacre studied the lungs from two dogs at two and almost four years after pneumonectomy.

Cournand[7, 21] indicated that in children and young puppies the cardiorespiratory function is almost as good after pneumonectomy as before, even under severe exercise. Longacre[16] studied animals from the same litter. Three of these he subjected to pneumonectomy at the age of one month. When ten months old the animals with one lung functioned as well as those with two lungs. However, three years later the animals with both lungs showed no change in cardiorespiratory function when subjected to severe exercise, whereas in those with only one lung there was considerable embarrassment of cardiorespiratory function. The animals did not, however, show the complete exhaustion demonstrated by the dog that had the pneumonectomy as a young adult animal almost four years previously. Both Longacre and Cournand arrive at practically the same conclusion believing that overdistention of the lung is more of a liability than an asset. Rienhoff[18] wrote, "We have been able to detect no evidence whatsoever that compensatory dilatation of the lung in either man or animal is harmful." It is generally agreed that the younger patient has less impairment of cardiorespiratory function following pneumonectomy than does the older patient. It requires little observation to realize that under normal condition of good health, with both lungs intact, children have better cardiorespiratory function than the older adults.

The results of overdistention of the lung studied five, ten, and fifteen years after pneumonectomy, with or without thoracoplasty, are so few in number that no unequivocal statement can be made concerning the necessity for preventing overdistention of the remaining lung by thoracoplasty or prosthesis. Some patients will develop cardiac decompensation, whereas others will develop pulmonary emphysema and show considerable cardiorespiratory distress even though one lung has not been removed. If the patient whose future held one or the other of these conditions were subjected to pneumonectomy surely he would show cardiorespiratory distress at some future time following the pneumonectomy. A patient, aged 53 years, nine years after a right pneumonectomy for carcinoma of the lung spontaneously claimed that breathing and the ability to engage in active occupations were better at that time than they had been three years before (Fig. 1).

To preserve cardiorespiratory function and prevent overdistention of the remaining lung Graham,[22] O'Brien,[23] Johnson,[4, 5] Skinner,[24] Alexander,[25] Cournand,[7, 21] and others thought that thoracoplasty should follow pneumonectomy.

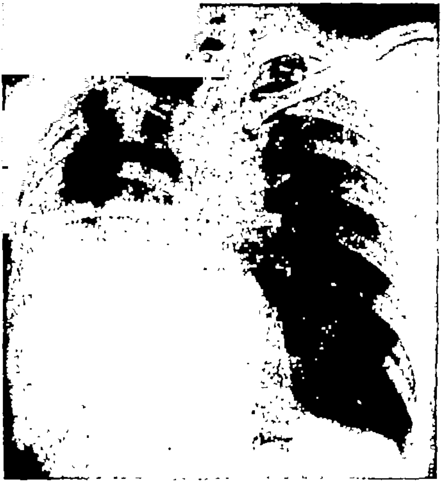


Fig. 1.—Roentgenogram of the chest of a white man, aged 53 years, whose right lung was removed for bronchiogenic carcinoma nine years before. This may be compared with Fig. 2, which shows a white woman, aged 33 years, with agenesis of the right lung.

Rienhoff,[19] Walker,[26] Overholt,[27] we, and others do not believe thoracoplasty is necessary after pneumonectomy for nontuberculous disease. Clinical observation would indicate that thoracoplasty is rarely necessary. It is possible that thoracoplasty may restore some lost function after the clinical course has indicated the development of impaired cardiorespiratory function. Graham[25] reported definite improvement in cardiorespiratory function following thoracoplasty in a patient with agenesis of the lung. Berry[7] wrote that thoracoplasty in a man aged 60 years promptly relieved symptoms of dyspnea after pneumonectomy. If thoracoplasty is needed after operation the differences in the right and the left lungs must be considered. The right lung has the greater volume. When it is removed the heart can move a greater distance than it can when the left lung is removed, because it quickly apposes itself to the left chest wall laterally.

One can turn to aplasia of the lung for an indication of what may be expected in a long-time survival without one lung. Patients with aplasia of the lung have been reported as dying from some other cause at the ages of 58 to 65 and 72 years.[29] We have diagnosed and observed a patient with aplasia of the lung 33 years of age. She has dyspnea under certain conditions but is able to carry on the usual duties of a graduate nurse (Fig. 2). The patient with agenesis of the lung has the equivalent of a pneumonectomy done when an infant. It has been shown that hyperplasia of the remaining lung occurs after pneumonectomy in young animals; however, in patients with agenesis of the lung, at autopsy six out of seven were reported to show emphysema of the lung. The patient who has a pneumonectomy as an adult cannot justly be compared with the patient who has agenesis of one lung.

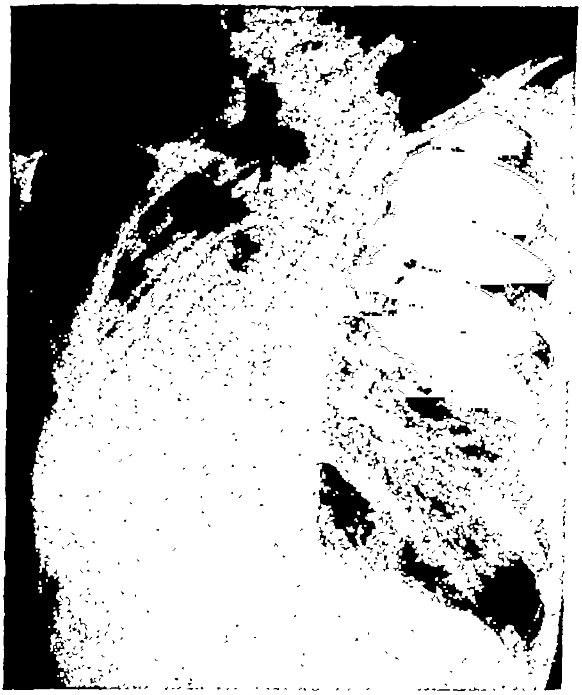
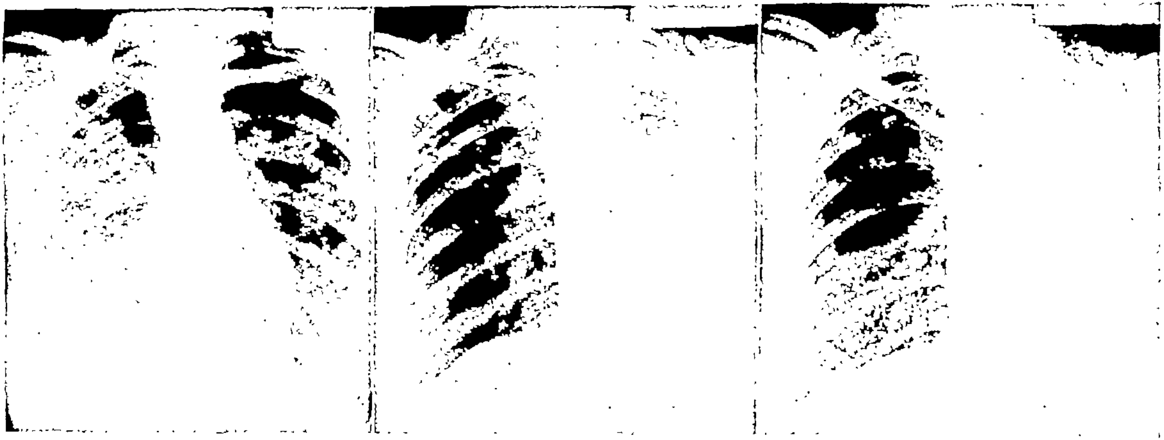


Fig. 2.—Roentgenogram of the chest of a white woman, aged 33 years, with agenesis of the right lung. She has dyspnea with exertion but is able to carry on the duties of a graduate nurse. This film should be compared with Fig. 1, which shows a chest nine years after right pneumonectomy for carcinoma of the lung.

Most surgeons who do pneumonectomy for tuberculosis believe that overdistention of the remaining lung enhances the flare-up of dormant or quiescent tuberculous lesions in that lung (Rienhoff,[19] Bailey,[30] Maier,[31] Overholt[32]). The thought is uppermost in the minds of thoracic surgeons doing collapse therapy in the treatment of tuberculosis, since the basis of collapse treatment is exactly the opposite of overdistention of the lung. In doing a lobectomy for pulmonary tuberculosis the surgeon has the opportunity of palpating the remaining portion of lung and more often than not small nodules can be palpated in the remaining lobe or lobes. When such lobectomies were not followed by thoracoplasty in our patients, the rate of flare-up or activation of the disease was rather high. Flare-up after lobectomy occurred in 30.8 per cent of 13 patients. On the other hand, at the time of pneumonectomy the surgeon has no opportunity of palpating nodules in the remaining lung and he



A. B. C.

Fig. 3.—Roentgenograms showing results of overdistention of the right lung in the natural course of pulmonary tuberculosis in a white woman, aged 33 years.

A, Bilateral disease was present in 1932.

B, This roentgenogram was taken in 1943, following sanatorium treatment. There has been definite destruction and contraction of the left lung. The right lung has healed considerably in spite of overdistention. Nevertheless, a cavity has developed in the upper lobe of the right lung.

C, Despite further contraction of the left lung and more overdistention of the right lung the cavity closed in 1945. The right lung remained quiescent or healed for three years, when a left pneumonectomy was done without a flare-up of the disease in the right lung. A pulmonary prosthesis was done and the patient has remained well for seventeen months.

is at liberty to assume that there is no disease in this lung. This may or may not be true. In our experience, however, 11 patients subjected to pneumonectomy for pulmonary tuberculosis who survived the operation remained entirely well from nine months to four and one-half years and have had neither thoracoplasty nor prosthesis following the pneumonectomy. It can be assumed that there were no lesions to become activated in the remaining overdistended lung or that overdistention is not important to the activation of the remaining dormant or quiescent lesions. In a study of patients with pulmonary tuberculosis it is not particularly unusual to see extensive disease on one side, with a gradual contraction of the lung and a gradual overdistention of the opposite lung. Frequently a lesion or even a cavity in the overdistended lung will heal (Fig. 3). A survey of such information merely emphasizes the fact that no unequivocal information is obtainable concerning the effect of overdistention upon healed, dormant, or quiescent tuberculous lesions.

Even though absolute facts are not known concerning the ill effects of overdistention upon healed, dormant, or quiescent tuberculous lesions, most thoracic surgeons believe that overdistention definitely enhances the activation or flare-up of such lesions. It is undoubtedly true that if one waits until there is a flare-up of a dormant or quiescent lesion, one has waited too long. It is much better to do a thoracoplasty before the disease has become activated than to attempt to cure the disease by thoracoplasty after the flare-up has occurred. Thus, the necessity for preventing overdistention of the remaining lung in the tuberculous patient after pneumonectomy seems far more important than it does to prevent overdistention of the remaining lung in the nontuberculous patient merely to prevent impairment of cardiorespiratory function of a clinical degree.

When the patient with pulmonary tuberculosis is facing the necessity of pneumonectomy, the risk of operation to the patient is far less than the risk of continuing with the disease without benefit of pneumonectomy. In other words, the patient is sick and any gamble on his life or future health is definitely in favor of the pneumonectomy. However, after the patient has survived the pneumonectomy for all intents and purposes he is well, and the risk of any contemplated prophylactic operative procedure may be greater than the danger of future disease that may occur in the patient. Therefore, the chances of an operative procedure are all against the patient. If thoracoplasty is contemplated the risk is slight but the deformity is considerable. In the event a safe, simple, nondeforming operative procedure could be developed, surely one would be justified in taking the risk to prevent future trouble to the patient. Lucite ball prosthesis is simple, easy, and nondeforming. The immediate risk is negligible. However, only time will determine its safety in future years.

Pulmonary prosthesis has not been used at the time of pneumonectomy in order to prevent additional possible harmful factors being introduced into the immediate postoperative period. It also seems rather difficult to determine how many Lucite balls would need be inserted if they were put in at the time of pneumonectomy. Therefore, in order to permit recovery at the time of pneumonectomy, and to allow the mediastinum to assume a normal position or one slightly shifted to the operative side, the Lucite balls are placed in the pleural cavity several weeks following pneumonectomy.

In the beginning the time interval from pneumonectomy to prosthesis was purely arbitrary. Rienhoff[33] indicated that fibrothorax may develop in five to forty-two days. Churchill[34] also believed that fibrothorax would develop. The first patient had a prosthesis three weeks after pneumonectomy. Later the time interval was increased to ten weeks. Fibrous tissue did not develop in any patient. It soon became evident that it would be much better to depend upon the position of the mediastinum and not upon time. Judgment based upon the position of the mediastinum is not infallible, however, since in some patients there is practically no thickening of the pleura and when the pleural cavity is opened the mediastinum has a tendency to shift too far to the unoperated side. On the other hand, in most patients the pleura is considerably thickened and there is no shift of the mediastinum. At the present time it seems rather difficult to determine preoperatively whether or not the pleura is thickened.

After pneumonectomy a permanent phrenic paralysis is done. This procedure is not carried out at the time of operation because the patient may desperately need the motion of the diaphragm in the immediate postoperative period. If the patient has survived uneventfully, the permanent phrenic paralysis is done at a separate operation in the cervical region approximately two to three weeks after pneumonectomy.

The operation of pulmonary prosthesis is carried out under local procaine anesthesia. The patient is placed in a lateral position with the pneumonectomy side uppermost. The incision is usually made over the third or fourth rib in about the anterior axillary line, making the incision between the pectoralis major muscle and the latissimus dorsi, since less tissue need be traversed in this region. A section of rib approximately one and one-half inches long is removed subperiosteally. The pleura is incised and a section of it taken for biopsy. The fluid in the pleural cavity is aspirated and cultured for pyogenic bacteria and tubercle bacilli. Enough Lucite balls are inserted to fill the pleural cavity. From nineteen to sixty-five have been used. The number of Lucite spheres needed depends upon the position of the mediastinum, the size of the patient, and whether it is the left or the right side. The Lucite spheres are sterilized in the manner described by Wilson but with slight modification. The spheres are immersed in 1:1,000 aqueous zepharin solution for eighteen to twenty-four hours. They are thoroughly rinsed in sterile saline and then placed on the instrument table in a solution of azochloramide, 1:3,300 in sodium tetradecyl sulfate, 1:500. The Lucite spheres are taken from the solution and deposited in the pleural cavity without drying.

Twenty-three patients have undergone Lucite ball prosthesis (Table I). There has been no immediate postoperative difficulty. However, for some unexplained reason it is not unusual for the temperature of these patients to be as high as 102° F. for several days. At first the unexplained fever was looked upon with a great deal of misgiving since it was well known that fever did not usually follow after Lucite ball plombage in the treatment of pulmonary tuberculosis. In this series of patients two have become infected. One patient showed a satisfactory postoperative period and was well for three weeks. At the end of this time he developed fever. Aspiration of the pleural space revealed frank pus, from which was grown *Staphylococcus albus hemolyticus* in pure culture. Tubercle bacilli could not be identified. For reasons beyond our control the patient was sent to another hospital, where he died approximately three weeks later without having the pleural space drained. At autopsy nothing abnormal was found except the empyema. There was no evidence of tuberculous lesions in the pleural cavity or the remaining lung.

TABLE I. PNEUMONECTOMY FOR TUBERCULOSIS; PULMONARY PROSTHESIS—LUCITE BALL

NAME	COLOR	SEX	AGE (YR.)	DATE OF PNEUMONECTOMY	DATE OF PROSTHESIS	END RESULTS TO 3/15/49
E. K.	C	F	?	9/ 2/47	10/ 6/47	Sputum negative, working 8 hours a day
J. S.	C	M	30	10/ 2/47	11/ 7/47	Dead, 5/18/48, no autopsy
W. O.	W	M	56	10/24/47	1/ 5/48	Dead, April, 1948, empyema
S. H.	W	F	35	11/17/47	1/10/48	Spread to contralateral lung, plombage contralateral side, sputum negative, condition good
G. C.	C	M	35	12/12/47	2/ 1/48	Condition good, sputum positive from contralateral disease, plombage contralateral
W. R.	C	M	39	12/19/47	2/ 7/48	Sputum negative, condition good
L. McK.	C	F	35	1/16/48	3/19/48	Sputum negative, condition good
G. L.	W	F	35	3/ 5/48	5/ 6/48	Sputum negative, condition good
E. P.	W	F	46	3/14/48	5/12/48	Sputum negative, condition good
A. S.	W	F	35	3/18/48	5/ 4/48	Sputum negative, condition good
J. C.	C	M	28	4/ 5/48	5/ 3/48	Sputum negative, condition good
J. D.	W	M	26	4/17/48	6/ 8/48	Sputum negative, condition good
L. A.	W	F	23	5/10/48	6/ 8/48	Sputum positive, low grade fever, bronchoscopy reveals endobronchial lesion of amputated stump
R. H.	C	F	24	5/14/48	7/27/48	Sputum negative, condition good
A. G.	W	M	46	7/ 9/48	9/ 9/48	Sputum negative, had empyema, being treated by aspiration and instillation, condition good
R. L.	W	F	26	7/23/48	9/10/48	Sputum negative, condition good
B. D.	W	F	29	9/ 7/48	11/ 4/48	Sputum negative, condition good
S. H.	W	F	23	9/20/48	11/ 4/48	Sputum negative, condition good
P. B.	C	F	17	10/ 1/48	12/13/48	Condition unknown
J. A.	W	F	34	10/18/48	12/ 3/48	Sputum negative, condition good
E. H.	W	F	23	10/29/48	12/22/48	Sputum negative, condition good
E. F.	C	F	22	10/26/48	1/13/49	Sputum negative, condition good
S. S.	C	F	15	11/16/48	1/10/49	Sputum negative, condition good

Another patient had a rather difficult postoperative period following pneumonectomy. Nine weeks after pneumonectomy a Lucite ball prosthesis was done. It was followed by a period of fever and then the temperature returned to normal. Eight weeks after the pulmonary prosthesis the patient began to have fever once again. The chest was aspirated; pus was found which contained only tubercle bacilli. He was first treated with aspiration and instillation of streptomycin, then penicillin, and finally aspiration and instillation of sodium tetradecyl sulfate, 1:3,300 and azochloramide, 1:500.[35] With the use of the latter solution the patient's temperature returned to normal, the appetite was good, he gained weight, and appeared to be rather well, but tubercle bacilli persisted in the aspirated fluid. The Lucite balls were easily removed by a small incision under local anesthesia. The incision was kept open for drainage. Thoracoplasty is contemplated for obliteration of the space and cure of the empyema.

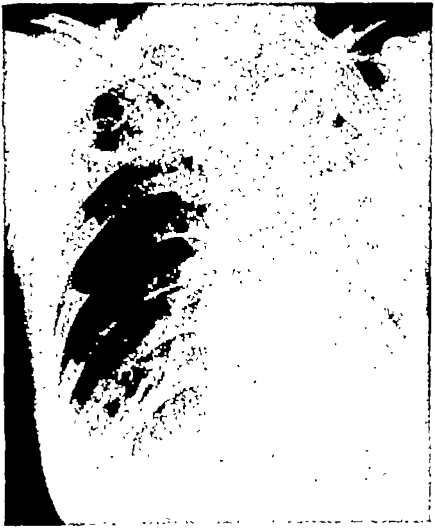


Fig. 4.—Roentgenogram showing the chest of a white woman, aged 33 years, whose left lung was removed for pulmonary tuberculosis. A pulmonary prosthesis followed in eight weeks. A cavity was noted in the apex of the right lung four and one-half months after pulmonary prosthesis. The patient was treated by bed rest and streptomycin for six weeks and then subjected to right pulmonary plombage. She has been well and has had a negative sputum for one year.

One patient of the group developed a cavity in the apex of the remaining lung after Lucite ball prosthesis. The cavity was closed by a Lucite ball plombage (Fig. 4). Another patient of the group was returned to the sanatorium and discharged as arrested, but six and one-half months after pneumonectomy the patient was brought into one of the local hospitals dead on arrival. One must assume that he died of pulmonary tuberculosis but no autopsy was obtained and it was impossible to determine the circumstances surrounding the death. The patients with Lucite ball prosthesis have been followed carefully from six months to twenty-two months.

In the beginning of the use of pulmonary prosthesis some misgivings were encountered when placing the Lucite balls on the left side of the chest against the pericardium, but no untoward effects have been noted from the use of the prosthesis on the left side. There have been fourteen prostheses on the left side and nine on the right. It is reasonable to assume that the heart is not beating against a harder structure than when it beats against the ribs or sternum.

The operation of pulmonary prosthesis has proved to be a simple, nondeforming operative procedure. However, the morbidity and mortality have been high when one considers that one patient out of twenty-three lost his life as a result of empyema following Lucite ball prosthesis and another patient developed what appeared to be a pure tuberculous empyema following Lucite ball prosthesis. It seems rather certain that routine thoracoplasty following pneumonectomy would be frought with less morbidity and mortality. It is possible, however, to rationalize somewhat concerning the high rate of mortality and morbidity. The patient who developed a pure *Staph. albus hemolyticus* infection of the pleural cavity was grossly contaminated at the time of his original pneumonectomy and was treated with sodium tetradecyl sulfate-azochloramide and sulfanilamide, and escaped infection of the pleural cavity.[36] However, at the time of prosthesis the biopsy of the pleura showed chronic inflammation of the pleural surface. Either this organism was dormant in the pleural cavity since the original operation or a contaminant was introduced at the time of operation. The second patient had a tuberculous empyema and was also grossly contaminated at the time of operation. The contamination probably contained tubercle bacilli as well as pyogenic organisms. He, too, was treated with azochloramide, sodium tetradecyl sulfate, and sulfanilamide mixture and escaped without infection of the pleural cavity. Again, it may be stated that the infection was dormant in the pleural cavity and flared up by the insertion of Lucite balls. The experience with these two patients leads to the conclusion that when the pleural cavity is by accident grossly contaminated at the time of pneumonectomy or when a tuberculous empyema is present at the time of pneumonectomy, the patient should not be subjected to Lucite ball prosthesis. Surely, in such patients if overdistention of the remaining lung is to be prevented thoracoplasty is the procedure to be followed.

Little information is obtainable concerning the incidence of pure tuberculous empyema or mixed infectious empyema occurring after pneumonectomy for tuberculosis. It seems highly probable that a certain number of empyemas will occur at a later date with or without thoracoplasty. In eleven pneumonectomies for pulmonary tuberculosis not followed by thoracoplasty one patient developed a pure tuberculous empyema six and one-half months after pneumonectomy (Table II). This is a higher incidence than with Lucite ball prosthesis.

TABLE II. PNEUMONECTOMY FOR TUBERCULOSIS; NO PROSTHESIS AND NO THORACOPLASTY

NAME	COLOR	SEX	AGE (YR.)	MONTHS SINCE OPERATION	SPUTUM NEGATIVE, PATIENT WELL	SPUTUM POSITIVE OR PATIENT SICK
K. McK.	W	F	44	55	Yes	–
W. M.	W	M	41	31	Yes	–
C. C.	C	F	26	30	Yes	–
J. K.	W	F	18	30	Yes	–
M. B.	W	F	19	29	Yes	–
C. G.	W	F	37	23	Yes	–
J. A.	C	M	32	17	Yes	–
J. B.	C	M	30	12	Yes	–
E. J.	C	F	31	11	Yes	–
P. S.	W	F	32	9	Yes	–
O. B.	W	M	31	9	Yes	–

It is assumed that with the additional information concerning pulmonary prosthesis now available the operation can be performed in the future with less mortality and morbidity. If the reduction in mortality and morbidity cannot be accomplished, then certainly the procedure should be abandoned in favor of thoracoplasty. Deformity should not influence the surgeon since it is his task to cure the disease.

The effect of the Lucite ball prosthesis in years to come cannot, of course, be known at this time.

SUMMARY

Pulmonary prosthesis with Lucite balls is a simple, easy, nondeforming method of preventing overdistention of the remaining lung after pneumonectomy.

The effects of Lucite ball prosthesis in years to come are yet to be determined.

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UNILATERAL LOSS OF COUGH REFLEX FOLLOWING COMPLETE AUTONOMIC DENERVATION OF THE LUNG FOR BRONCHIAL ASTHMA

CASE REPORT

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KUMMELL,[1] in 1923, first reported immediate relief of asthma by unilateral cervical sympathectomy. He postulated the vagus as being the chief motor nerve to the lung, but fearing the consequences of vagotomy, attacked the cervical sympathetics, believing that some of the motor fibers of the vagus were transmitted via this pathway. His idea was to diminish bronchospasm by weakening its innervation. Later, Braeucker, in Kummell's clinic, demonstrated that stimulation of either the vagus or sympathetic produced at times an increased resistance to air exchange. Subsequently, many continental surgeons began excising various segments of the cervicodorsal sympathetics with extremely variable results, as might be expected. This is not surprising in view of the variance in case selection, no less than the divergent operative procedures employed. Even from the very brief operative descriptions sometimes given it is evident that many of these sympathectomies were incomplete. Braeucker stated that even with complete removal of the stellate ganglion, sympathetic stimulation reaches the homolateral lung, as rami communicantes send fibers from as low as the fourth thoracic root.

The year following Kummell's original report, Kappis[2] reported equally encouraging immediate results from vagotomy on the right side, below the emergence of the recurrent laryngeal. The seeming paradox of relief of asthma by the interruption of two systems having predominantly antagonistic motor effects was then explained on the basis of the reflex arc, of which the sympathetic was the afferent and the vagus the efferent limb. Dixon and Brodie[3] had reached this conclusion following electrical and pharmacologic stimulation of cut nerve endings in experimental animals, and stated that the vagus was the chief bronchoconstrictor nerve, and the sympathetics the chief bronchodilator. Furthermore, these efferent components were demonstrated to be linked to afferent arcs which completed the reflex: bronchodilation following stimulation of afferent fibers in the central cut ends of the vagi, and conversely, bronchoconstriction following stimulation applied to the central cut end of the sympathetic.

There is by no means any universal agreement as to the physiology of pulmonary innervation. Phillips and Scott,[4] in an excellent review of the surgery of asthma, stated that the theory of the sympathetic being the afferent limb of

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a reflex arc was "theoretically attractive without many known facts for its foundation." They question the infallibility of Dixon and Brodie's conclusions on nerve stimulation, because the studies were carried out in animals having a combined vagosympathetic trunk. However, they conceded that all the extrinsic nerve paths controlling bronchiolar caliber were eventually condensed in the posterior pulmonary plexuses. They felt that if the beneficial result of surgery could be attributed to the interruption of a reflex with multiple and complicated afferent-efferent pathways, then section of both motor and sensory channels would more likely produce a good result. It is worth while to note, however, that the bronchial walls themselves contain numerous ganglion cells and a complicated intrinsic nerve network, not unlike the intestinal plexuses of Auerbach and Meissner. In this connection, Drinker[5] made the pertinent observation that complete denervation of the lung is quite impossible.

Despite the lack of agreement on the fundamental physiology, the surgery of asthma has been based on the concepts outlined. Sympathectomy has been advocated to block the afferent pathway over the stellate and upper thoracic ganglia. The efficacy of such surgery would, of course, depend upon a complete interruption of the afferent arc. Leriche and Fontaine[6] reported relief from stellectomy alone, but others believed that a wider operation including the upper thoracics is necessary. Levin,[7] in asserting that the sympathetics constitute the chief bronchoconstrictors of the lung, observed the necessity for removing (or destroying by alcohol injection) the third, fourth, and fifth thoracic ganglia which contribute direct branches to the pulmonary plexus. Moreover, he described indirect branches from all the thoracic ganglia, via the aortic plexus. Miscall and Rovenstine,[8] subscribing to the concept of the sympathetics as the afferent limb of a reflex arc, favored sympathectomy in those patients in whom asthma was felt to be due to vagal overactivity. They noted the procedure of posterior pulmonary plexus resection as advocated by Rienhoff and Gay, but warned that this procedure might disturb reflexes essential to normal respiration. Rienhoff and Gay,[9] however, in reporting eleven patients upon whom this procedure had been done, stated flatly that there had been no postoperative complications. The following case report is therefore offered, not to evaluate the efficacy of the procedure described in the treatment of asthma, but rather to point out an interesting and important complication, namely, the clear-cut and unilateral loss of the cough reflex following both sympathetic and vagal denervation. The procedure had been selected on the basis of the arguments as given by Phillips and Scott.

CASE REPORT

M. R. M., a 40-year-old white woman, entered National Jewish Hospital on July 29, 1949, with chief complaint of bronchial asthma of sixteen years' duration. The patient stated that she had been a frail child and had had typhoid fever at the age of 6 years. She had had tonsillitis and chorea at 14 years of age, and was told by a physician, in 1936, that she had "leakage of the heart."

Asthmatic history dated back to March, 1933, and began with an acute, unheralded attack while she was a college senior. She had two more asthmatic attacks in the same year, and subsequent to these, she began to experience a constant cough that was slightly productive of white foamy sputum, but she had no wheezing. In the period from 1934 to 1938, she received a great deal of therapy for sinusitis and nasal polyps, but had no severe asthmatic attacks. In 1938, she had two episodes of status asthmaticus for which she was hospitalized, and treated with oil-ether retention enemas. After 1938, the asthma was intermittent and irregular, and the patient described it as annoying rather than disabling. The patient observed that in the period from 1939 to 1943, during which time she had three pregnancies, the asthma was definitely less severe. In the summer of 1945, the attacks became more intense and more frequent, and she was using adrenalin freely. In 1946, she had an episode of status during which she was hospitalized for a period of twenty-three days, and again in 1947, she was hospitalized with severe asthma and a superimposed pneumonitis. From this time on she experienced almost constant asthma, and was unable to carry on her housework. She then sought surgical relief, and on Feb. 10, 1949, a right cervicodorsal sympathectomy was done, followed two weeks later by the same procedure on the left. On each occasion the stellate and first two thoracic ganglia were removed. After the first procedure she felt very much better, but after the second stage the brief sense of well-being declined and she again began to have asthma. Because of the persistent and severe attacks, it was suggested that a complete autonomic denervation be done, and she entered the National Jewish Hospital for this purpose.

Physical examination revealed an emaciated white woman in obvious respiratory distress, with a wheeze which was audible across the room. The accessory muscles of respiration were called into play, and stood out as visible cords in the neck. The chest was tympanitic to percussion; breath sounds were loud with an increased expiratory duration. There were numerous crackling râles and wheezes over the entire chest. There was no cardiac enlargement. The pulse was 84 and regular. A soft blowing murmur was heard early in diastole. The blood pressure was 104/84.

The red blood count was 5,160,000 with 14 Gm. of hemoglobin. White count was 14,200 with 72 per cent neutrophils, 24 lymphocytes, 3 eosinophils, and 1 basophil. Urinalysis revealed a specific gravity of 1.018 with one plus albumin.

A posteroanterior roentgenogram of the chest showed findings of pulmonary emphysema.

The maximum breathing capacity was 43.5 liters per minute. The resting arterial oxygen saturation was 84 per cent and the average pulmonary arterial blood pressure during cardiac catheterization was 22 mm. Hg. (A more complete résumé of the objective pulmonary and cardiac findings is intended for a later report.)

Bronchoscopy revealed some blunting of the carina, and a velvety thickened appearance of the bronchial mucosa.

On Aug. 17, 1949, under ether-endotracheal anesthesia, and through a right transpleural approach, the vagus nerve was isolated below the recurrent laryngeal, and all communicating branches to the root of the lung were resected to the level of the inferior pulmonary vein. The vagus was transplanted into the pleural cavity. The sympathetic chain was then mobilized at the point of its previous resection above the third dorsal ganglion, and was resected below the seventh thoracic ganglion. Two No. 45 French right-angle drains were placed in the pleural cavity, and the chest closed in layers.

A postoperative film on Aug. 23, 1949, showed a wedge-shaped area of atelectasis at the right base along the right heart border. Bronchoscopy at this time revealed thick, tenacious material in the orifices of the right lower lobe segments. It was also noted that the patient had no cough while the right side of the bronchial tree was being examined. With the thought that this might be a fortuitous finding due to the passage of the cocaine solely into the right bronchial tree, bronchoscopy was repeated on August 30, limiting anesthesia to the pyriform sinuses and cords by swab application. The findings were quite striking: a complete absence of cough while examining and aspirating the right bronchial tree, and the immediate elicitation of persistent cough when the tip of the bronchoscope crossed the carina into the left main-stem bronchus. Bronchoscopy was repeated on September 3, with identical findings. Bronchoscopy was not completely effective in clearing the atelectasis in the right base, and for this reason a Métras catheter was passed into the right anterior basal segment bronchus every other day. Following the passage of the catheter, 4 c.c. of saline containing 100,000 units of penicillin, 0.1 Gm. streptomycin, and 0.5 c.c. of 1:1000 adrenalin was instilled, and the bronchus was aspirated. On this regime, the atelectasis cleared almost completely.

From September 24, the patient again began to experience severe asthma and was in status on several occasions. However, she showed satisfatory response to the intravenous administration of 10 c.c. of 1 per cent Novocain, repeated at intervals. It was decided in view of the unhappy result on the right side to limit surgery on the left to vagal stripping. This was carried out on October 7, through the left transpleural approach. The postoperative course was marked by mild disorientation for two days, following which the patient had an uneventful recovery.

A follow-up bronchoscopy on Oct. 23, 1949, revealed essentially the same findings as previously noted. The cough on the left side had not been changed by vagal stripping alone.

DISCUSSION

If the sympathetics and the vagus constitute a reflex arc mediating the bronchodilating and bronchoconstricting reflexes, it is logical to assume that other important reflexes are likewise so transmitted, and complete autonomic denervation will lead to profound changes.

The procedure employed in this patient has left her prey to atelectasis and pneumonitis on the right side. Follow-up observation two months after the first procedure revealed a persistent and clear-cut absence of cough on the right, and considering the technique employed in transplanting the vagus intrapleurally, it is doubtful whether return of function will occur. On the other hand, stripping of the vagal fibers to the posterior pulmonary plexus appears to be an innocuous procedure as far as preservation of cough is concerned, as Rienhoff and Gay have definitely stated.

No attempt has been made in this report to evaluate the status of the patient's asthma following bilateral denervation. It is felt that this will require a more prolonged observation during which time a close watch will be kept over the patient's pulmonary status with particular emphasis on the right lung. In the future, we intend limiting denervation to the vagal side of the autonomic arc in view of the untoward complication in this patient.

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METASTATIC PULMONARY MALIGNANCY: A STUDY OF FACTORS INVOLVED IN EXFOLIATION OF MALIGNANT CELLS

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THE finding of malignant cells in the sputum of patients suffering from primary bronchiogenic carcinoma is being reported with increasing frequency, and its value as a diagnostic tool in this condition is well established. Secondary tumors of the lung, involving the bronchi as they not infrequently do, might also be expected to exfoliate malignant cells in the sputum. The purpose of our study was to determine whether or not malignant cells can be recovered in the sputum of patients suffering from metastatic tumors of the lung and to examine the factors responsible for exfoliation of these malignant cells.

REVIEW OF THE LITERATURE

The use of cytologic examination of sputum as an aid to the diagnosis of primary pulmonary neoplasm received little attention until the introduction by Dudgeon and Wrigley[1] of the "wet-film" technique. They examined sputum in 58 cases, in 38 of which the diagnosis of bronchiogenic carcinoma was subsequently established. Malignant cells were found in the sputum from 26 (68 per cent) of these 38 patients. Subsequent reports[2-14] on the use of this method have indicated a percentage of correct diagnoses ranging from 60 to as high as 92.5 in some more recent series. Incorrect diagnoses occur but become less and less frequent as the examiners become more familiar with the technique. Woolner and McDonald[14] reported that a falsely positive diagnosis was made in approximately 2 per cent of 300 consecutive cases in which sputum examinations gave positive results. The frequency with which thoracotomy is being initiated when cytologic examination of sputum has given the only definite pathologic evidence of the disease testifies to the fact that this diagnostic method is considered to be highly accurate. It is generally felt that a diagnosis of bronchiogenic carcinoma can be made on the basis of findings at bronchoscopic examination in approximately 50 per cent of cases. Cytologic study of the sputum and bronchial secretions may be expected to increase the number of accurate preoperative diagnoses by at least 20 per cent.

The finding of malignant cells in the sputum of patients suffering from secondary pulmonary tumors has been mentioned only rarely in the literature. Betschart,[15] as early as 1895, reported 2 cases of metastatic osteogenic sarcoma in which malignant tissue was found in the sputum. There were 3 cases of metastatic pulmonary neoplasms in Dudgeon and Wrigley's[1] series in 2 of which the sputum contained malignant cells. Barrett[2] found malignant cells in the sputum of 9 patients who had secondary tumors of the lung. He predicted that exfoliation of malignant cells in the sputum might be expected in cases of hyper-

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nephroma and sarcoma with pulmonary metastatic lesions. It was emphasized by Gloyne[16] that almost any type of malignant cell, squamous, polygonal, or columnar, might be found in the sputum in cases of secondary tumors of the lung. Cells from carcinoma of the esophagus and pharynx were the most common. Gowar,[3] on the other hand, reported 5 cases of secondary neoplastic growths of the lung in which examination of the sputum gave negative results.

Wandall[4] in an extensive review of the subject of neoplastic cells in the sputum reported positive findings in the sputum of 8 patients who had metastatic pulmonary neoplasms, and negative results in 4. Those who had positive sputum included 2 who had carcinoma of the colon, 2 who had hypernephromas, 1 who had carcinoma of the breast, 1 who had a parotid tumor, one tumor of the testis, and one osteogenic sarcoma. It was his feeling that the primary or secondary nature of a tumor of the lungs could not be determined from cytologic study of the sputum as the two are frequently similar histologically. Exceptions were cases of metastatic hypernephromas of the kidney, seminomas of the testis, and sarcomas. In these instances, he felt that the cell types were sufficiently distinctive so that they could be recognizable in the sputum as being different from cells exfoliated from primary bronchiogenic carcinoma. Others[6, 7, 9, 10] have reported the occasional finding of malignant cells in the sputum in cases of secondary tumors of the lungs.

The reliability of cytologic examination of sputum in the diagnosis of metastatic pulmonary malignancy cannot be determined from the reports mentioned because not enough cases were encountered by any author to be considered significant, and no consistent attempt was made to list the negative results as well as the positive ones. McKay and associates[10] encountered less success in recovering malignant cells from the bronchial secretion of cadavers with secondary tumors of the lung than of those with primary bronchiogenic carcinoma. Zimmerman and Lubliner[17] made the statement that in their experience, tumor cells have not been found in the bronchial secretions of patients with pulmonary metastatic lesions in spite of the fact that erosion into the bronchi by metastatic tumors can and does occur.

The fact that bronchial involvement may occur in cases of secondary tumors of the lung has been emphasized in recent years as the bronchoscope has come into more widespread use, and it is no longer a rare occurrence for secondary tumors to be seen through the bronchoscope and for the diagnosis to be made after examination of a specimen obtained through the bronchoscope.[18-24] King and Castleman[25] investigated the frequency of bronchial involvement in metastatic pulmonary malignant lesions in 109 cases at necropsy. In 20 (18.3 per cent) bronchial invasion by malignant cells was found, the invasion in 11 being noticeable grossly. They emphasized that no special effort was made to search carefully for small metastatic mucosal nodules and stated furthermore that the sections disclosing microscopic involvement of the bronchi were taken at random only. Had a more careful search been made, undoubtedly the percentage of cases of secondary pulmonary tumors with bronchial involvement would have been higher. In a recent review of pulmonary resection for metastatic malignancy[26] it was found that the question of bronchial involvement was mentioned in 27 of 62 cases reported in the literature. In 17 (63 per cent of these 27 cases or 27 per cent of the entire series) bronchial involvement was present. Seiler[26] concluded that the actual percentage of bronchial involvement was between 35 and 40.

MATERIAL AND METHODS

In order to determine whether or not malignant cells can be found in the sputum of patients with metastatic pulmonary lesions and to determine as nearly as possible the accuracy of this diagnostic method, the case records of *patients whose sputum and bronchial secretions had been examined for malignant* cells at the Mayo Clinic were reviewed.

Two groups of cases were included in the study. The first group consisted of 400 cases in which examination of sputum and bronchial secretions for carcinoma cells gave positive results. These were reviewed and the number of cases of proved or suspected metastatic pulmonary tumors tabulated. Only cases in which a tissue diagnosis of a primary malignant lesion elsewhere in the body had been made were listed as "proved cases." If a malignant tumor had been removed at another hospital but no tissue was available for study or if the clinical and roentgenographic findings indicated that a malignant tumor was present elsewhere in the body but resection was not carried out because of the presence of pulmonary metastasis, the condition was listed as suspected but not proved. Cases of lymphosarcoma, or carcinoma of the larynx, pharynx, and esophagus, were excluded as not being true metastasis.

A second group of cases was reviewed and handled similarly. This group consisted of 488 miscellaneous cases in which examination of sputum or bronchial secretion was performed and gave negative results. These cases were encountered during the same period of time that 100 cases were reported by the laboratory as having malignant cells in the sputum or bronchial secretion.

Because of our findings in these groups, a pathologic study was made of lungs removed at operation and at necropsy in cases of secondary tumors of the lung. Sections were made through the bronchi which were grossly involved with tumor tissue, and paraffin sections were made for microscopic study. For purposes of comparison similar sections of primary bronchiogenic carcinoma, bronchial adenomas, and cylindromas were studied.

RESULTS

In the group of 400 cases in which sputum or bronchial secretions were reported positive for malignant cells were 16 cases of metastatic pulmonary malignancy. In 8 of these the diagnosis was proved by resection of the primary tumor and examination of tissue, in 6 it was strongly suspected because of clinical and roentgenologic findings, and in 2 the diagnosis was questionable since the site of the suspected primary tumor was unknown, although the roentgenograms of the thorax were considered by the roentgenologist to be typical of pulmonary metastasis. These 16 cases included 8 cases of carcinoma of the breast and 1 each of carcinoma of the colon, carcinoma of the cervix, malignant teratoma of the testis, carcinoma of the prostate, papillary carcinoma of the thyroid, and carcinoma of the ovary. In the remaining 2 cases, the site of the suspected primary tumor was unknown.

Of 488 patients who had miscellaneous conditions in which cytologic examination of the sputum was reported negative, 30 were believed to have metastatic tumors of the lung. In 17 of these the diagnosis was proved by examination of tissue, in 10 it was strongly suspected, and in 3 the site of the primary malignancy was unknown. Of the 100 patients whose sputum was reported as positive during the period in which these 488 patients were examined, 4 were considered to have metastatic tumors of the lung. Thus, out of a total of 34 patients who had proved or strongly suspected metastatic pulmonary malignancy, 4 were found to have malignant cells in the sputum and the remaining 30 did not; this gives a percentage accuracy of 11.8.

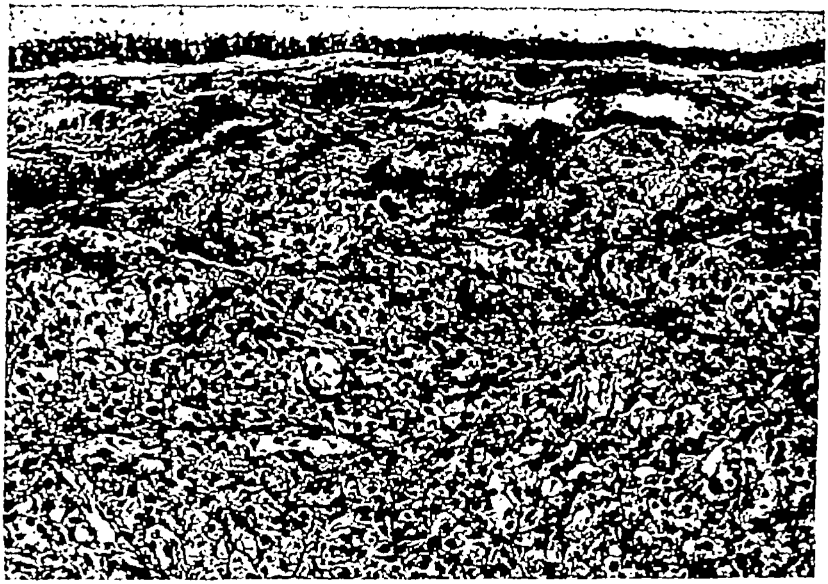

Fig. 1.—Metastatic adenocarcinoma involving bronchial wall. Intact surface mucosa may be noted (hematoxylin and eosin, x115).

From these results, it would appear that exfoliation of carcinoma cells in the sputum is a rather rare occurrence in metastatic pulmonary malignancy. The relative infrequency of bronchial mucosal involvement by metastatic tumor is undoubtedly responsible to a certain extent for the comparatively low incidence of malignant cells appearing in the sputum. Even with gross bronchial involvement, metastatic malignant tumors are unlikely to exfoliate cells. This fact was brought out clearly in reviewing the case records of patients with metastatic tumors of the lung whose sputum and bronchial secretions were negative for carcinoma cells. In 7 of these cases a specimen obtained through the bronchoscope proved to be malignant tissue, in 6 of these 7 cases a definite polypoid tumor was visible bronchoscopically. In 3 additional cases, in which resection was carried out, gross bronchial involvement was evident in the specimen in spite of which repeated sputum examinations had been negative. In

2 cases from which malignant cells were recovered in the bronchial washings, repeated examinations of sputum had been negative and the malignant cells were recovered only after the bronchial mucosa had been disturbed by bronchoscopic biopsy procedure. These findings suggest that when bronchoscopic biopsy

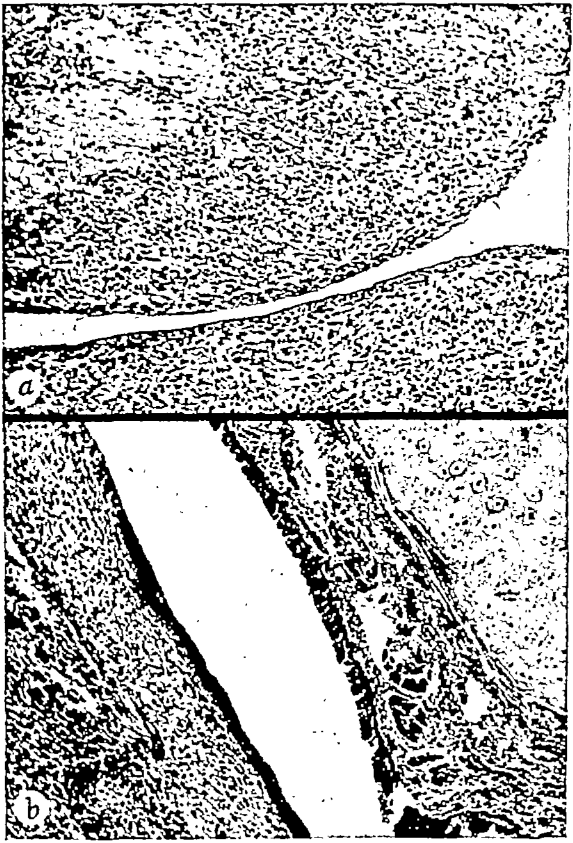

Fig. 2.—Metastatic sarcoma involving the bronchial wall. *a.* The surface epithelium overlying the tumor is flattened but still intact (hematoxylin and eosin, ×100). *b.* The bronchial epithelium has undergone squamatization (hematoxylin and eosin, ×100).

is positive and a definite polypoid tumor is visible through the bronchoscope and yet repeated examinations of sputum and bronchial secretions are negative for carcinoma cells, the lesion may be metastatic in origin.

Unfortunately, the cells exfoliated by secondary pulmonary neoplasms encountered in this study were not sufficiently distinctive to indicate their secondary origin. Even in retrospect we were unable to determine the secondary nature of the exfoliated cells seen in the sputum of patients suffering from secondary pulmonary tumors. It might be said, however, that if squamous cells or small cells are found in the sputum, the chances that the tumor is primary in the lung are excellent, as these cells are rarely seen in cases of metastatic malignant lesions of the lungs.

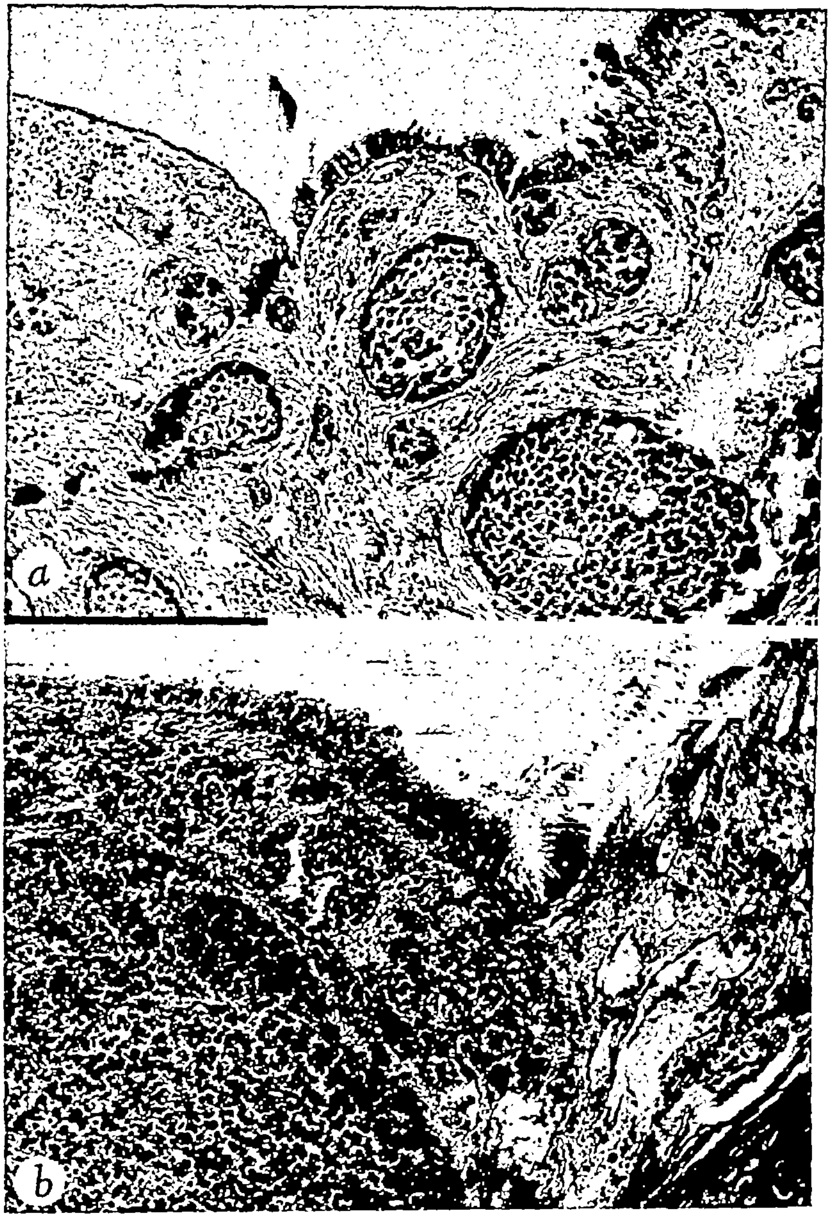

Fig. 3.—Metastatic carcinoma of bronchial wall. *a*. Microscopic foci of tumor in bronchial mucosa (hematoxylin and eosin, *x100*). *b*. Edge of polypoid tumor mass projecting into bronchial lumen. The surface mucosa is intact in both cases (hematoxylin and eosin, x115).

PATHOLOGIC STUDY

These observations led us to examine more carefully the lungs removed at operation and at necropsy in cases in which secondary pulmonary tumors were present. Our purpose was to determine if possible what factor or factors might be responsible for the infrequent occurrence of malignant cells in the sputum of these patients.

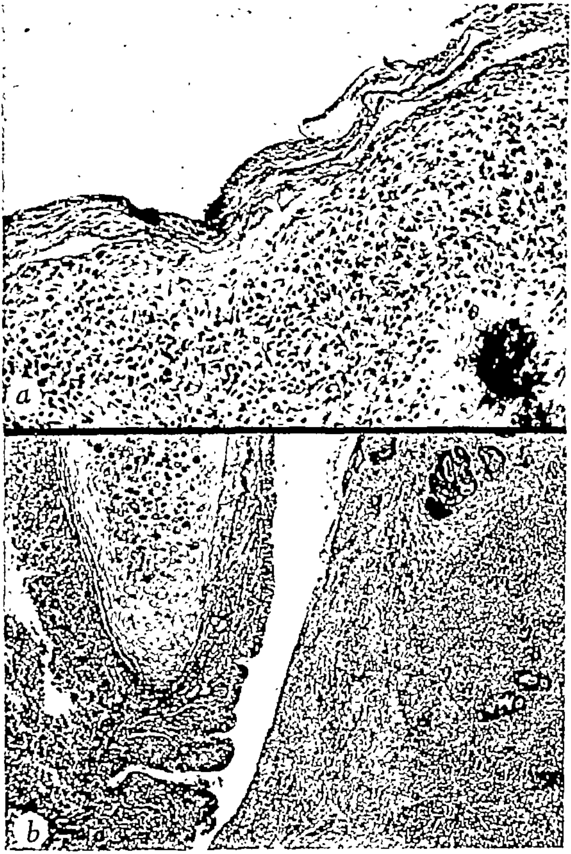

Fig. 4.—Metastatic malignancy of bronchial wall. *a.* The polypoid tumor mass is covered by a layer of hyalinized connective tissue (hematoxylin and eosin, ×100). *b.* A zone of necrotic material separates the tumor from the bronchial lumen (hematoxylin and eosin, ×32).

The most striking finding was the frequent observation that the bronchial epithelium maintained its integrity over the surface of the metastatic tumor even in the face of extensive bronchial involvement (Fig. 1). The epithelium was frequently found to be flattened (Fig. 2, *a*) and in some areas to have undergone squamatization (Fig. 2, *b*), but its function as a protective epithelial covering was maintained and for this reason there was little opportunity for malignant cells to exfoliate.

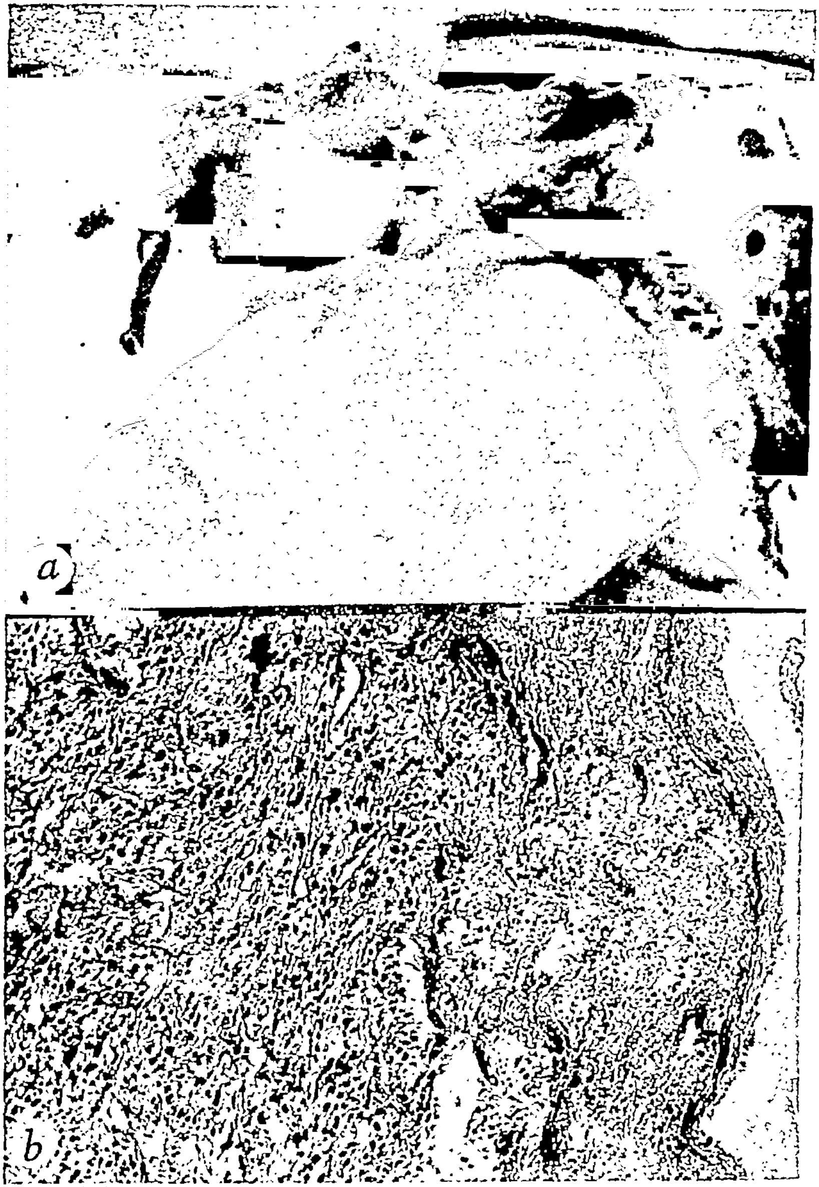

Fig. 5.—Metastatic fibrosarcoma to lung. *a*. Specimen showing polypoid mass projecting into bronchial lumen. *b*. Histologic section through the polypoid tumor (hematoxylin and eosin, ×100).

Early and late stages of bronchial involvement by metastatic carcinoma are shown in Fig. 3, *a* and *b*. The bronchial mucosa shown in Fig. 3, *a* contains multiple microscopic foci of metastatic carcinoma. The metastatic tumor tissue shown in Fig. 3, *b* had produced a polypoid tumor mass measuring 3.5

cm. in diameter. In both instances the surface mucosa remained intact and the examination of sputum was negative for carcinoma cells.

In certain cases a polypoid metastatic nodule was found in the bronchial wall with loss of the overlying surface epithelium. Failure to obtain malignant cells in the sputum was explained in 1 case (Fig. 4, *a*) by a layer of acellular connective tissue over the tumor and in another (Fig. 4, *b*) by a thick zone of necrotic material overlying the metastatic malignant tissue.

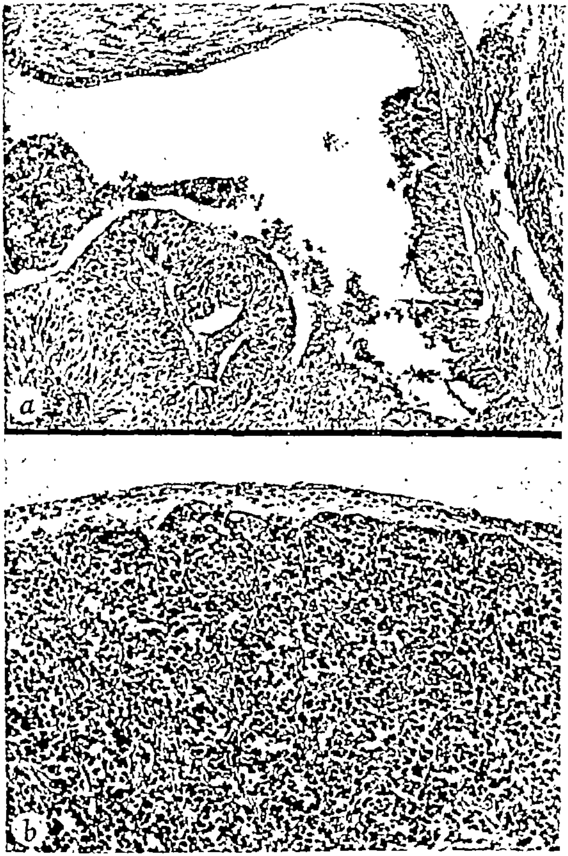

Fig. 6.—*a*, Primary bronchiogenic carcinoma, squamous-cell type, showing malignant change in surface epithelium. Carcinoma cells can be seen free in the lumen of the bronchus (hematoxylin and eosin, x85). *b*. Bronchial adenoma. Note the flattened but intact epithelial lining over the tumor (hematoxylin and eosin, x135).

Tissue from a surgically resected fibrosarcoma with a polypoid projection into the bronchial lumen is shown in Fig. 5, *a*. A section through the polypoid tissue (Fig. 5, *b*) revealed a thick zone of necrotic tissue on the surface of the tumor which precluded the finding of malignant cells in the sputum.

For purposes of comparison, a histologic section through the wall of a bronchus in a case of primary bronchiogenic carcinoma is shown in Fig. 6, *a*. Since these tumors arise from the surface epithelium of the bronchus, every opportunity exists for the exfoliation of cells into the lumen from the free surface of the tumor. On the other hand, examination of sputum in cases of bronchial adenomas and cylindromas has yielded consistently negative results. These tumors, however, arise from the subepithelial mucous glands and an intact epithelial covering can usually be demonstrated over the surface (Fig. 6, *b*). The findings on pathologic examination, therefore, are essentially the same in cases of bronchial adenomas and cylindromas as in many cases of metastatic malignant tumors to the bronchus.

SUMMARY

The finding of malignant cells in the sputum in cases of metastatic pulmonary neoplasms is a relatively infrequent occurrence.

Of 400 cases in which sputum was found to contain malignant cells, 16 were cases of metastatic pulmonary neoplasm. Among 488 cases in which miscellaneous conditions were present and examination of the sputum for malignant cells was negative were 30 cases of metastatic pulmonary neoplasms. Of 100 patients whose sputum was reported as positive during the period in which the 488 patients were examined, 4 were considered to have metastatic tumors of the lung. Thus, the percentage accuracy of sputum diagnosis among 34 cases of metastatic tumors of the lung was 11.8.

The pathologic explanation for the low incidence of positive results on sputum examination in secondary pulmonary tumors derived from this study is that the surface epithelium remains intact over the metastatic bronchial lesion in many cases. A covering of necrotic tissue in some cases and a protective acellular connective tissue layer in others prevent recovery of malignant cells in the sputum as often as would be anticipated, when the not infrequent occurrence of bronchial involvement in cases of secondary pulmonary tumors is considered.

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EXPERIENCES WITH THE USE OF DIRECT AORTOGRAPHY IN THE DIAGNOSIS OF COARCTATION OF THE AORTA

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ADVANCES in the surgery of congenital cardiovascular defects have stimulated the development of more accurate methods of diagnosis. Coarctation of the aorta does not usually present any diagnostic difficulties. It is made clinically upon the presence of symptoms of hypertension, differences in blood pressures and pulses in the upper and lower part of the body, and roentgenologic evidence of notching or erosion of the inferior borders of varying numbers of ribs. In most instances, the site of the coarctation is immediately distal to the origin of the left subclavian artery. However, it occurs occasionally in another part of the aorta, or, in the infantile type, several centimeters of aorta may be involved in the coarctation. It is thus to the advantage of the surgeon to know as much as possible about the exact nature and location of the defect before operation is attempted.

Roentgenologic contrast visualization gives more information about these lesions than any other diagnostic procedure, and is carried out by the injection of a radiopaque substance into the cardiovascular system while serial roentgenograms are rapidly taken.

Methods for contrast visualization of the aorta include:

1. *The intravenous injection of Diodrast as developed by Robb and Steinberg.*[1] This gives excellent visualization of the superior vena cava and right chambers of the heart. However, after the opaque media has passed through the pulmonary vascular bed, it is frequently diluted to such an extent that proper contrast is not achieved in the aorta, and the point of stricture, therefore, not clearly outlined.

2. *The retrograde injection of Diodrast through the left common carotid artery, as has been used by Freeman*[5] *and Stevens,*[2, 5] *Burford and Carson,*[3] *and others.* This method gives greater contrast and more detail than any of the others. However, exposing the carotid artery would seem a rather formidable procedure to be used in the performance of a diagnostic study. There is likewise the possibility of injury to that artery, which in certain cases might result unfavorably.

3. *The introduction of an intravenous catheter into the ascending aorta through the right or left radial artery with the retrograde injection of 70 per cent Diodrast as described by Broden and associates*[4] *and Crafoord.*[5] Adequate visualization of the coarctation is usually obtained. However, a relatively large amount of contrast substances is required, because much of it is dissipated

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through the left common carotid and left subclavian arteries before the coarctation is reached. Also, there is the possibility of occluding the orifice of one of the coronary arteries with the tip of the catheter.

We have employed a method only slightly different from the third mentioned, but it appears to present advantages in some respects, and it is for that reason that it is being reported. This method utilizes the left radial artery and permits the tip of the catheter to enter the descending rather than the ascending aorta. The greatest concentration of opaque material is thus placed directly at the point of coarctation and permits the use of a much smaller amount.

TECHNIQUE

Before the procedure is performed, 1 c.c. of a solution of 1 part 70 per cent Diodrast in 10 c.c. of saline is injected intravenously to determine whether or not the patient is sensitive to it. Nembutal and morphine sulfate are given one hour before starting. The patient is placed supine upon a fluoroscopic table and the anticubital fossa and volar surface *of the left forearm prepared and sterile drapes applied. Under local 1 per cent Novocain* anesthesia, a diagonal incision about 2 to 3 cm. in length is made beginning at the anticubital fossa and extending distally over the course of the radial artery. This artery is exposed and dissected distally to its first large tributary. A ligature is placed distally on this tributary and it is occluded proximally by means of a small bulldog arterial clamp. A transverse incision is made in the occluded portion and the proximal lumen dilated with a mosquito forcep. The tip of a regular size 9 or 10 intravenous catheter, through which heparinized physiologic saline is running, is then introduced into it (Fig. 1). Thereupon, the bulldog clamp is removed and the catheter rapidly passed until it meets a slight resistance. This indicates that the tip of the catheter has reached the abrupt downward turn of the subclavian artery into the mediastinum or the coarctation itself, and can easily be determined by fluoroscopy at this time. If the former has occurred, the catheter is withdrawn for several centimeters, the arm abducted to about 90°, and another attempt is made to pass the catheter. This is usually successful and the tip is positioned just within the lumen of the aorta (Fig. 2). If the coarctation has been reached, the catheter is withdrawn to a similar position. One should be extremely careful to avoid forcibly passing the catheter through any region of resistance.

When the proper position has been achieved, the patient is turned on the left side and a preliminary lateral film is taken. If this is satisfactory, 25 c.c. of 70 per cent Diodrast are then injected as rapidly as possible while seven serial films are exposed at intervals of about one second by means of an automatic cassette changer. If good visualization of the coarctation is not obtained, the necessary adjustments are made and the injection repeated, a total of not more than 75 c.c. being given during the entire procedure. A ligature is then placed about the artery while an assistant withdraws the catheter. The skin and subcutaneous tissues are closed with interrupted sutures. Upon returning to the ward, penicillin is begun and the arm elevated. Little discomfort is associated with the procedure. Immediately after injection of the contrast substance, there is a momentary substernal burning sensation followed by a generalized hot flush which lasts from one to three minutes.

RESULTS

From Jan. 1, 1949, to May 1, 1949, thirteen patients with coarctation have been subjected to the procedure in this clinic. One other had no angiographic study, because of a severe allergic reaction after the injection of the test dose of Diodrast. This patient's history revealed previous, mild asthmatic attacks. Nine of the patients were adequately visualized, were thought to present only the

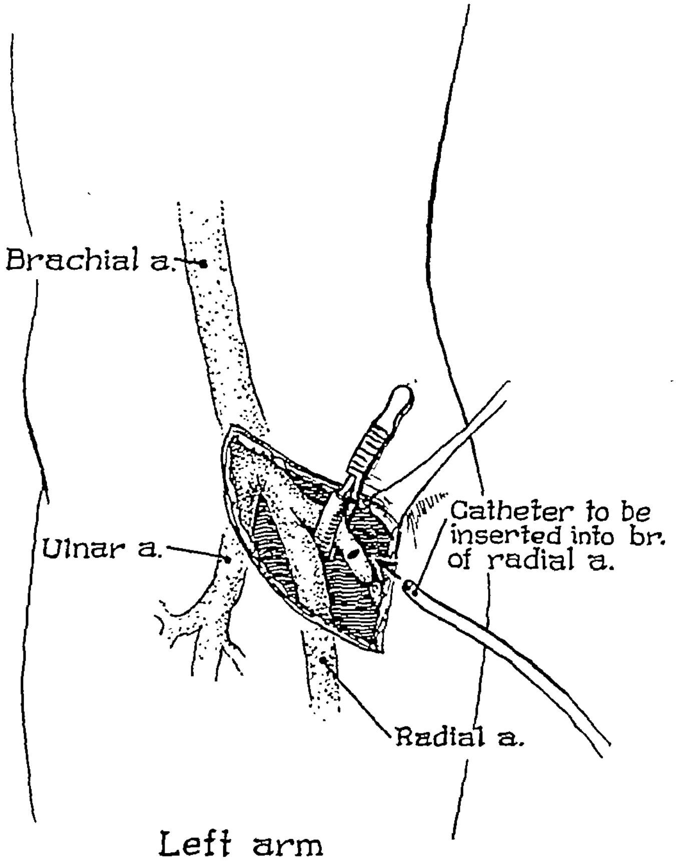

Fig. 1.—Diagrammatic drawing of the arteries of the left forearm. A segment of the first large branch of the radial artery has been occluded and a transverse incision made in it. The tip of the catheter is inserted into the incision and passed up the brachial artery to the aorta.

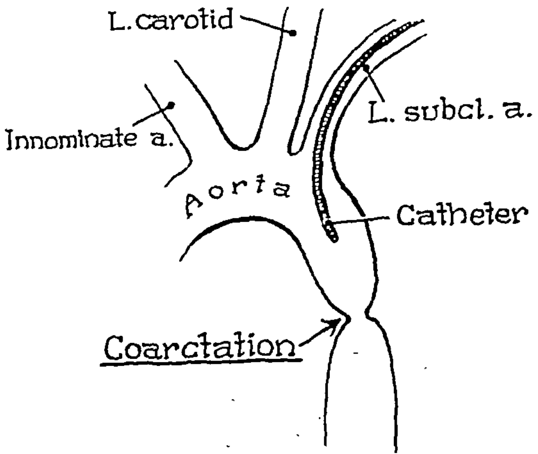

Fig. 2.—Diagrammatic illustration of the aortic arch and coarctation of the aorta, demonstrating the proper position of the tip of the catheter relative to the coarctation.

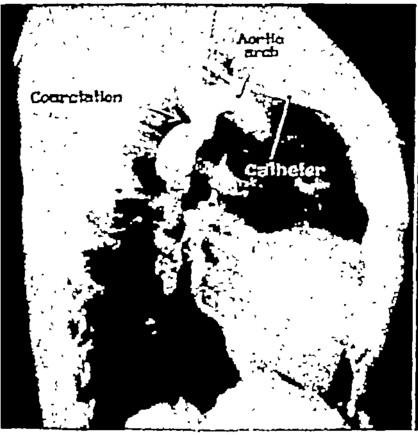

Fig. 3.

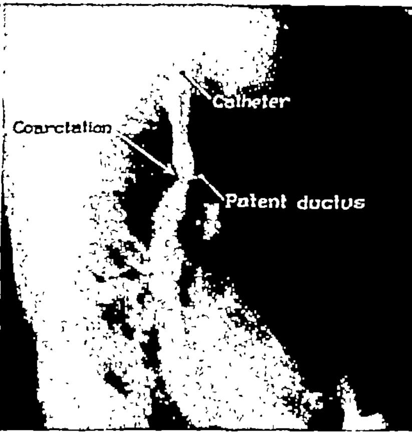

Fig. 4.

Fig. 3.—Aortogram showing type of coarctation most frequently encountered. Left subclavian artery, aortic arch, and collateral circulation are also demonstrated.

Fig. 4.—Aortogram demonstrating patent ductus arteriosus associated with coarctation of aorta.

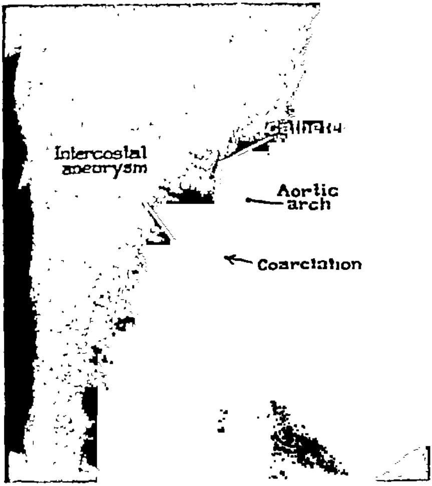

Fig. 5.—Aortogram demonstrating aneurysm of intercostal artery immediately below area of coarctation of aorta.

usual type of coarctation, and were found at operation to be essentially the same anatomically as represented in the aortograms (Fig. 3). In one of the remaining four, a patent ductus arteriosus could be seen (Fig. 4). The fact that this was known before operation had no influence upon the actual manner in which it was performed. In one there was an aneurysm of the left first intercostal artery (Fig. 5) which could be seen preoperatively on the aortogram. In another, aneurysms of both first intercostal arteries were found at operation which were not visualized on the aortogram. It was thought that failure to visualize them was due to the fact that a relatively far posterior position caused them to be obscured by the adjacent vertebral bodies, and also because the patient was quite large and obese. In still another, a 10-year-old boy, a dissecting aneurysm in the segment of aorta immediately distal to the point of coarctation was present at operation, but could not be seen on the aortogram. Examination of the specimen after operation revealed no defect or evidence of trauma in the intima of the proximal or distal aortic segments of the coarctation. However, the aneurysm appeared to be of recent origin, and because no other cause for its presence could be determined, it was assumed to be related to the catheterization. Successful resection with an end-to-end anastomosis was carried out.

DISCUSSION

This method of aortography is not necessarily presented as the one which gives the most detailed x-ray visualization. However, it does have several distinct features to recommend its use. First of all, it is technically simple to perform and does not require specialized instruments other than the catheter. It is of minimal discomfort to the patient, and a general anesthetic is not required except in small, uncooperative children. Because the left radial artery and consequently the descending aorta is catheterized, the possibility of the tip of the catheter entering the orifice of one of the coronary arteries with its attending consequences is not present; also a smaller amount of opaque substance is required, and the greatest concentration is placed at the site of the coarctation. However, on three occasions the tip of the catheter passed through the coarctation and it was necessary with a strain gauge manometer to determine by means of the differential pressure relationships that existed as the catheter was slowly withdrawn, the proper position above the coarctation at which its tip should remain. Although we have in most cases employed an automatic rapid casette changer, and its use is highly desirable, the procedure may be carried out on any routine x-ray machine by exposure of a single film just before the injection of the contrast substance is completed. There have been no convulsions, paralysis, or other untoward reactions associated with the procedure except for a mild febrile reaction in the first two cases. They were found to be due to the presence of pyrogens in improperly cleaned catheters and upon correction of this, no additional reactions were encountered.

The method's disadvantages include poor or no visualization of the ascending aorta and first part of the aortic arch. Also, the resistance offered by the catheter to fluid on injection is greater than that occurring with a short cannula of the same caliber. Thus, a slower rate of injection of the opaque substance occurs. Finally, if the catheter is passed injudiciously there is some possibility of injuring the wall of the vessel.

It is felt that the simplicity of the procedure, the minimal amount of danger and discomfort to the patient, and a high degree of assurance of obtaining adequate demonstration of the defect warrants its use in all patients with suspected coarctation who are not sensitive to the contrast substance.

SUMMARY

1. Coarctation of the aorta is usually easily diagnosed. However, the point of stricture may occasionally occur in some portion of the aorta other than immediately distal to the left subclavian artery and is best demonstrated by contrast radiography.

2. A method of catheterization of the left radial artery and descending aorta followed by injection of 25 c.c. of 70 per cent Diodrast is presented. Using a small amount of opaque material a high level of concentration is placed at the point of coarctation and adequate roentgenologic contrast visualization of this defect and other abnormal vessels in the immediate vicinity is achieved.

3. The procedure has been performed upon thirteen patients with coarctation of the aorta from Jan. 1, 1949, to May 1, 1949, at the Johns Hopkins Hospital with adequate demonstration of the anatomic defects before operation.

4. The advantages and disadvantages of the method are discussed.

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ARTERIOVENOUS FISTULA OF THE LUNG

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ARTERIOVENOUS fistulas in the peripheral circulatory system are not uncommon surgical problems particularly in the fields of traumatic and miliary surgery. Their pathogenesis, systemic complications, and surgical management are well understood, and the latter is usually attended with a great degree of success. Similar fistulas, however, in the pulmonary circulatory system are rare, and until recent years neither a correct clinical diagnosis had been reported nor a successful surgical procedure performed upon them. Although they must occur with more frequency than the literature would indicate, they have not been widely recognized.

The first case of a cavernous hemangioma associated with secondary polycythemia was reported by Rodes[1] in 1938. The patient was a 25-year-old man who had cyanosis, clubbing of the fingers and toes, polycythemia, and x-ray evidence of nodules in the mid-portion of the left lung field. The patient suffered from intermittent attacks of hemoptysis and eventually died of a massive pulmonary hemorrhage. The post-mortem examination showed two cavernous hemangiomas on the right and one on the left. Other, similar, nonoperated cases have been described by Smith and Horton[2] and Sisson and associates.[3] Characteristic findings in the clinical histories were the presence of cyanosis of the skin and mucous membranes and clubbing of the fingers. The polycythemia and marked elevation of the hemoglobin content of the blood were other notable observations.

The first successful surgical removal of such a lesion was recorded by Hepburn and Dauphinee[4] in 1942. The patient was a 23-year-old woman who had had cyanosis and clubbing of the fingers and toes for eight years. Red blood cell count varied between 9 and 9.6 million per cm., and the hemoglobin content of the blood between 21.8 and 22.8 Gm. per hundred c.c. The roentgenograms of the chest showed an infiltrating lesion in the middle and lower lobes of the right lung. A total pneumonectomy was performed. A year later the clubbing had disappeared, and the patient was reported to be normal.

Three reports of patients treated successfully with surgery appeared in 1944. Janes's[5] patient had hemangiomatous tumors in both lungs, and a total of four of them were removed by local resection at two operations. The patient of Adams, Thornton, and Eichelberger[6] was treated by a left pneumonectomy because of masses in both lobes of the lung. Jones and Thompson[7] did a right pneumonectomy. The absence of a middle lobe and of a superior pulmonary vein made their problem unique.

Pathologically, two of these first four surgically removed lesions exhibited cavernous sinuses and dilated vascular channels lying in a mass beneath the

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visceral pleura. One showed multiloculated cavities with smooth linings communicating with small arteries and veins, and another, a branch of the enlarged pulmonary artery terminating in a cavity with a smooth lining, 7 by 7 by 8 cm. in size, branches from which communicated with the inferior pulmonary vein through superficial varicosities.

Several other cases have recently been reported in which the pulmonary lesions have been resected.[5-14] Since there are still problems in this abnormality which are not yet clearly understood, the following two surgically treated patints are presented.

CASE REPORTS

CASE 1.—The patient was an unmarried woman, aged 30 years, who was seen on Aug. 2, 1946, complaining of shortness of breath. The illness at the time she was seen had started six years previously with an attack of right-sided pneumonia with, however, only a mild systemic reaction. An x-ray examination of the chest had at first been reported to show a neoplasm, but the subsequent films did not confirm this impression. Shortly thereafter she developed mild dyspnea which became slowly but steadily more serious and culminated, six weeks previous to the first visit, in dyspnea and orthopnea so severe that she could not work and could not lie down to sleep. She was also somewhat cyanotic and had mild edema of the ankles. She was successfully treated with digitoxin and rest, and at the time of the first visit was comfortable under ordinary conditions of activity.

For many years she had had a mild chronic cough, productive of a small amount of clear, mucoid sputum and in recent weeks a persistent mild temperature elevation. There was no history of pulmonary osteoarthropathy.

Past History.—The patient had had pneumonia in the right lung at the age of 16 years following an appendectomy. A postoperative ventral hernia had been repaired on two different occasions. There had been no other serious illnesses, accidents, or operations.

Family History.—Her mother had died of carcinoma of the uterus. A maternal aunt had died of carcinoma of the intestine and a maternal uncle of carcinoma of the liver. There was no history of familial telangiectases.

Physical Examination.—The temperature was 99.6° F. The pulse rate was 96 a minute. The respiratory rate was 18 a minute. The blood pressure was 140 mm. of mercury, systolic, and 70, diastolic. The patient was an obese, white woman who did not appear ill. There was no cyanosis. The skin was clear. The head, eyes, ears, nose, throat, and neck were normal. The thorax was symmetrical. There was no tenderness. The breasts were normal, and the chest expansion was normal. The breath sounds were normal on the left; they were slightly suppressed at the right base anteriorly, laterally, and posteriorly. There were no râles. In the region of the right anterior axillary line, extending from a point high in the axilla to the base and anteriorly and posteriorly as well, there was a loud, harsh bruit, synchronous with systole of the heart and markedly accentuated with deep inspiration. There was no thrill. The heart was not enlarged clinically. The heart sounds were regular and rhythmical without murmurs. There was a firm, surgical scar in the right lower quadrant of the abdomen. The liver was palpable but not tender. The spleen and kidneys were not palpable. There was no abdominal tenderness, and there were no masses. There was no clubbing of the fingers and toes or edema of the ankles. The weight was 172 pounds.

X-Ray and Fluoroscopic Examination.—Roentgenogram of the chest taken in July, 1946 (Fig. 1, *A* and *B*), showed minimal cardiac enlargement, an unusually large right pulmonary artery, and a rounded mass at the right base anteriorly. Fluoroscopically the artery was unusually active. Pulsations were thought to be present in the mass. A diagnosis was made of a probable arteriovenous fistula in the lower lobe of the right lung.

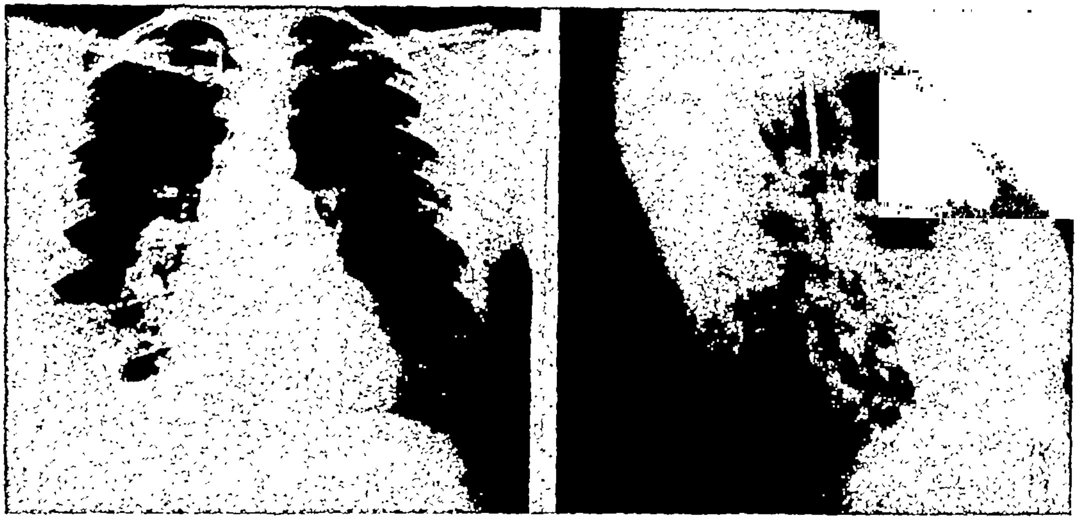
The patient was placed on an antiobesity diet and admitted to the hospital on Sept. 17, 1946, having lost twenty pounds. Condition and general physical examination otherwise were the same as when she was first seen.

Laboratory Examinations.—The red blood cell count was 4.6 million per c.mm.; hemoglobin content of the blood was 14.5 Gm. per cent; white blood cell count was 8,800 cells per c.mm.; arterial oxygen content was 19.40 volumes per cent; arterial CO_2 content was 43.90 volumes per cent; and the total blood volume was 5,320 c.c., the plasma volume being 2,818 c.c., and the cell volume 2,502 c.c.

The electrocardiogram showed a right axis deviation.

Bronchography.—Bronchograms of the right lung showed normal bronchial filling without displacement of any of the bronchial segments.

Bronchoscopy.—There was slight reddening of the mucous membranes in the right bronchial tree, but all bronchial orifices were normal with no displacement or rotation.



A. *B.*

Fig. 1, *A* and *B* (Case 1).—Posteroanterior and right lateral chest films. A shadow in the right lower lung field is apparent. The large vessel leading to it from the right hilum could be seen pulsating violently when the patient was examined fluoroscopically.

Operation.—A right lower lobe lobectomy was done on Sept. 24, 1946. Cyclopropane anesthesia was used with sodium pentothal and curare as induction agents. The pleural cavity was entered through the bed of the seventh rib. There were friable, filmy adhesions throughout the pleural space. In the anterior basilar segment of the right lower lobe there was a soft pulsating mass, 7 cm. in diameter. A rough thrill was palpable in it. Both the inferior pulmonary vein and the right lower lobe artery measured 3 cm. in diameter. A lobectomy was done without difficulty. Between the time when the artery was divided and the vein ligated, but not yet divided, the aneurysmal sac became more full and tense suggesting that the bronchial artery contributed to its filling. The bronchial artery was .75 cm. in diameter. The operation was uneventful. A catheter for drainage was left in the pleural cavity at the end of the operation.

Postoperative Course.—The postoperative course was satisfactory. The drainage tube was removed on the third day. The red blood cell count varied between 3.35 and 3.72 million per c. mm. and the hemoglobin content of the blood between 9.5 Gm. per cent and 11.5 Gm. per cent. The patient was discharged from the hospital at the end of the second week in good condition.

Gross Pathology.—The specimen consisted of the right lower lobe of the lung (Fig. 2). On cut section there was a cystic space in the anterior basilar segment of the lower lobe, 6 cm. in diameter, that had a thin wall and a smooth glistening lining. The basilar segment branch of the lower lobe artery was 1.5 cm. in diameter. It coursed behind the cyst to its inferior portion where it opened directly into it. Another branch of the artery also opened into it after pursuing a devious course through pulmonary tissue. The cystic structure had a direct opening into the inferior pulmonary vein.

Microscopic Pathology.—The wall of the artery showed thickened and hypertrophic media, and the wall of the sac resembled vein.

Hospital Readmission.—The patient returned to the hospital on Jan. 12, 1947, stating that for two weeks she had had a nonproductive cough, right-sided chest pain, ankle edema, and intermittent fever, all of a mild degree. On examination there was no cardiac enlargement, and the sounds were regular and rhythmical, but there was an inconstant, harsh, faint, systolic murmur audible only in the aortic area and transmitted to the vessels of the neck. Both lungs were clear to percussion and auscultation. The liver was 3 cm. below the costal margin in the midclavicular line and was slightly tender.

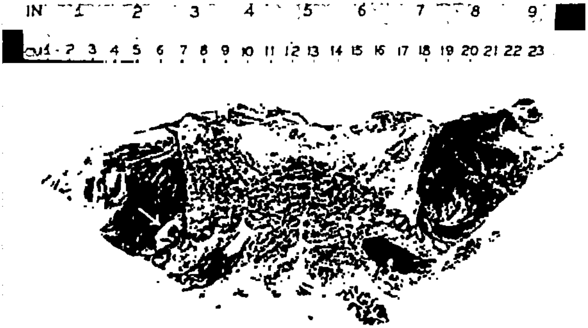

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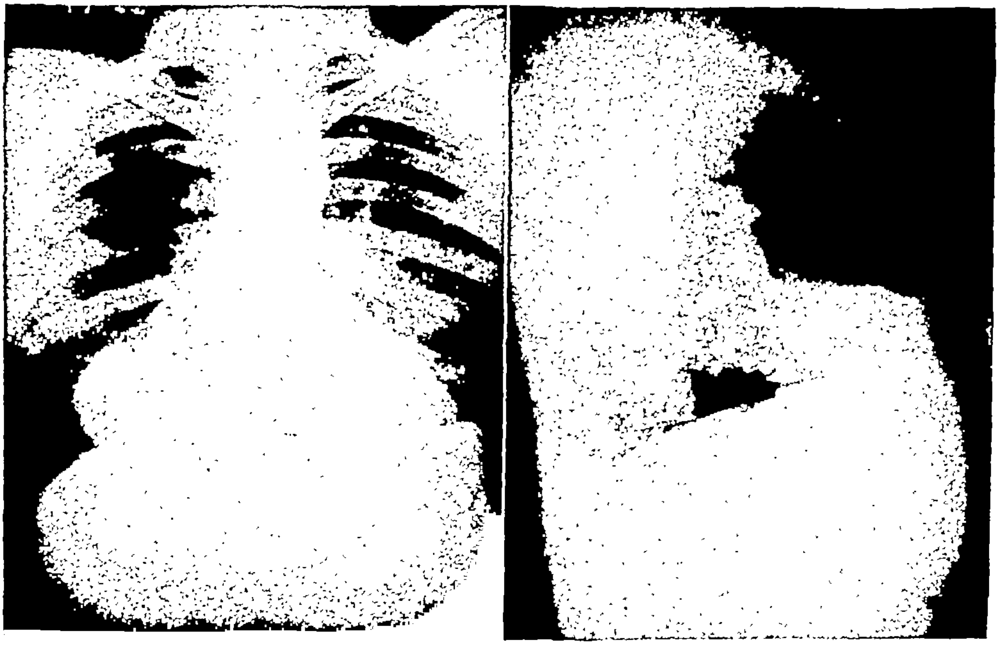
Fig. 2 (Case 1).—Gross specimen. The right lower lobe has been cut and opened like a book. The large vessel adjacent to the sac is the lobar artery. The arrow indicates the opening of the sac into the inferior pulmonary vein.

X-ray examinations of the chest showed a heart of normal size. There was a prominent rounded bulge in the right hilar region, probably the stump of the lower lobe artery. There was cloudiness in the region of the right costophrenic sulcus and the right diaphragm was slightly higher than normal. The electrocardiogram was normal. The red blood cell count was 5.5 million cells per c. mm. of blood, and the hemoglobin content was 16.5 Gm. per cent. During the hospital stay the patient had no fever, cyanosis, edema, elevation of the white blood cell count, cough, or chest pain, and was discharged three days later. She has remained in good health, but the murmur persists.

Case 2.—The patient was a 50-year-old white man who was admitted to the hospital on Jan. 15, 1947, without specific complaints. During the course of a pre-employment physical examination a roentgenogram of the chest was taken on Nov. 11, 1946, which showed a tumor of the right lung. The patient denied cough, dyspnea, orthopnea, hemoptysis, weight loss, cyanosis, or fever. He had had rare episodes of constricting pain in the right anterior chest lasting one to two minutes and radiating to the right midaxillary region.

Past and Family History.—These were irrelevant. Of note, however, was the fact that the patient had worked as a laborer without difficulty for many years. There was no history of familial vascular tumors.

Physical Examination.—The temperature was 98.6° F. The pulse rate was 90. The respiratory rate was 18. The blood pressure was 110 mm. of mercury, systolic, and 70, diastolic. The patient was well developed and nourished. The skin was clear. There was cyanosis of the skin of the face, hands, and mucous membranes which was accentuated when the patient was in the recumbent position. The head, eyes, ears, and nose were normal. There were moderate dental caries and severe pyorrhea alveolaris. The neck was normal. The chest was barrel-shaped. Expansion was symmetrical. Anteriorly, on the right, there was dullness to percussion below the level of the fourth rib with decreased breath sounds and vocal fremitus. There was a bruit in the right chest anteriorly audible from the second to the fifth rib and laterally to the anterior axillary line. It was synchronous with systole of the heart, its intensity varied from day to day, and it was accentuated by deep inspiration. There was no thrill. There were fleeting, dry, crackling râles at both bases. The heart was not enlarged. The sounds were regular and rhythmical without murmurs. The abdomen was soft and flat throughout without tenderness or masses. The liver, spleen, and kidneys were not palpable. The rectum was negative. There was a soft, translucent mass, 3 cm. in diameter, at the upper pole of the left testicle. Slight clubbing of the fingers and toes was present. The weight was 170 pounds.



A. *B.*

Fig. 3, *A* and *B* (Case 2).—Posteroanterior and right lateral chest films. The shadow is in the vicinity of the right middle lobe.

Laboratory Examinations.—The laboratory data were as follows: the red blood cell count was 6.16 million per c.c. of blood; white blood cell count was 6.200; hemoglobin content was 19.5 Gm. per cent; serum total proteins were 7.3 Gm. per cent; hematocrit was 64; circulation time (calcium gluconate in right basilic vein to the tongue) was eleven seconds; venous blood CO_2 was 49.75 volumes per cent; venous O_2 was 9.48 volumes per cent; arterial CO_2 was 42.15 volumes per cent; arterial O_2 capacity was 25.67 volumes per cent; arterial O_2 content was 22.75 volumes per cent; arterial blood oxygen saturation was 88.6 per cent of normal; total blood volume was 8,780 c.c.; cell volume was 5,135 c.c.; the plasma volume was 3,645 c.c.; respiratory quotient was .622; the coefficient of O_2 utilization was 56.3; venous pressure was 200 mm. of water and the vital capacity was 4.3 liters.

X-Ray and Fluoroscopic Examination.—Roentgenogram of the chest (Fig. 3) showed an oval tumor mass in the anterior portion of the right lower lung field, probably in the middle lobe, and an enlarged blood vessel passing to it from the hilum. Fluoroscopically, the mass could be seen to pulsate and the artery was unusually active.

Angiograms were done on two different occasions (Fig. 4, *A* and *B*). Fifty cubic centimeters of 70 per cent Diodrast were employed each time, and the films were taken immediately after the injection and at one and two seconds later. The Diodrast passed immediately *into the mass, intensifying its shadow and outlining the artery wall. In addition, a* second vessel, presumed to be vein, could be seen passing between the hilum and the mass.

Bronchoscopy.—This procedure contributed little except that it showed redness of the mucous membrane in the right bronchial system and broadening and blunting of the major carina.

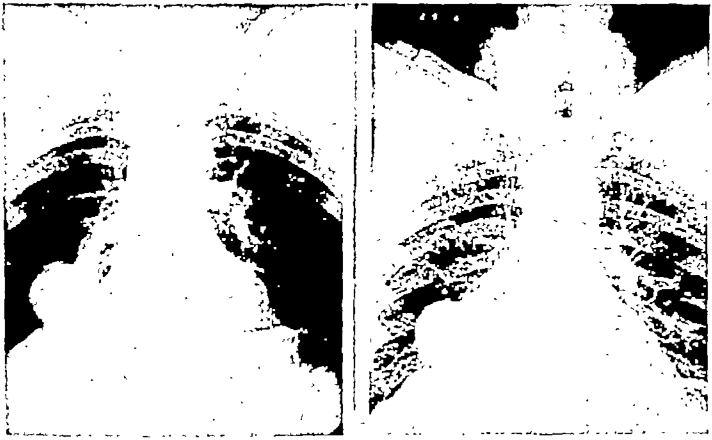

A. *B.*

Fig. 4 (Case 2).—*A*, This exposure was taken one second after the Diodrast had been injected. The Diodrast is beginning to pass through the sac and demonstrates two blood vessels leading to it.

B, One second later. The Diodrast has accentuated the sac and has passed into the smaller pulmonary vessels.

Operation.—A thoracotomy was performed on Feb. 4, 1947. A cystic structure, measuring 5.5 by 6 by 8 cm. in size, lay immediately beneath the pleura in the anterior portion of the middle lobe. A thrill was palpable in it and waves could be seen passing through it with each systolic contraction of the heart. The superior pulmonary vein measured 3 cm. in diameter. Because of the large size of all the branches of this vein, suggesting that there might be a branch of the upper lobe artery entering the aneurysm, and because of the proximity of the sac to the horizontal interlobar fissure it was decided it would be best to remove both the upper and middle lobes. This was done without difficulty. An intercostal catheter was placed into the pleural cavity for drainage at the conclusion of the procedure.

Postoperative Course.—The patient developed a serious atelectasis in the right lower lobe on the first postoperative day that required repeated intratracheal aspirations before it was controlled. Ultimately the lower lobe expanded well, and at the time of the patient's discharge from the hospital three weeks later, it had completely filled the right thoracic cavity. *The catheter was removed on the third postoperative day. The temperature reached* normal on the tenth postoperative day. At the time of discharge the red blood cell count was 5,590,000 per c. mm.; the hemoglobin content of the blood was 15.9 Gm. per cent, and the hematocrit was 49.8.

One month later the patient returned to the hospital with jaundice thought to be due to a delayed serum reaction from the blood transfusions administered at the time of the operation. It cleared slowly, and the patient has remained well until the present time.

Gross Pathology.—A unilocular cyst occupied a large part of the middle lobe and compressed the surrounding pulmonary tissue (Fig. 5). The middle lobe could be dissected from the upper lobe without difficulty and there were no vessels extending from the upper lobe into the cyst as had been feared at operation. The middle lobe artery was 6 mm. in diameter. It entered the superior portion of the lateral wall of the cyst. The middle lobe vein was 1 cm. in diameter. The intima of the artery showed slight atheromatosis.

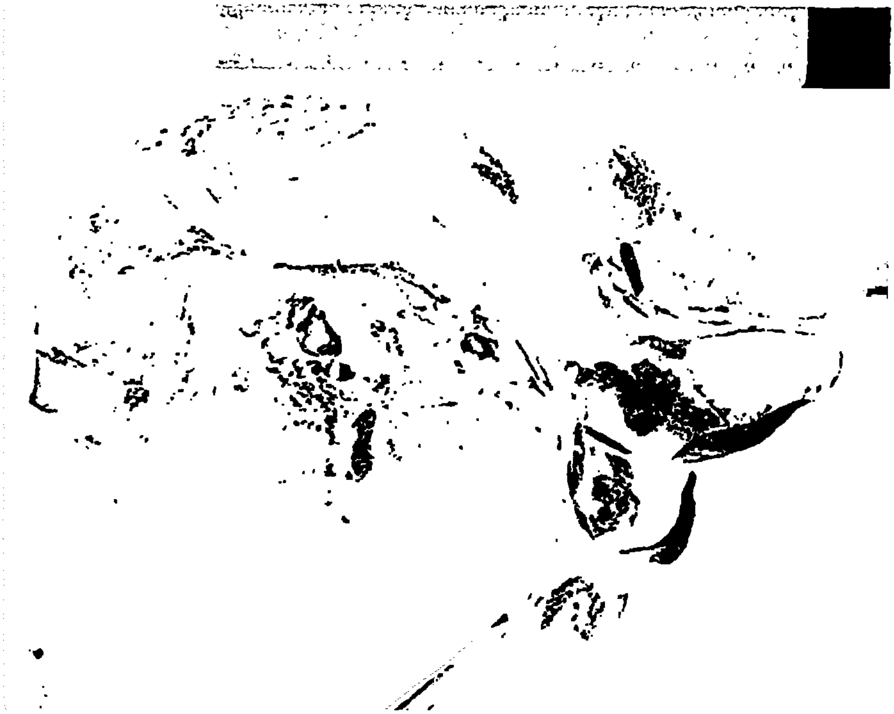


Fig. 5 (Case 2).—Gross specimen. The upper lobe is on the left, the middle lobe on the right. The lower left indicator passes through the arterial branch to the sac and the upper right through the venous.

Microscopic Pathology.—The wall of the arterial branch to the sac was essentially normal. However, near the expanded portion of the sac the normal smooth muscle of the artery disappeared and was replaced by fibrous connective tissue except for occasional bundles of smooth muscle and a few elastic fibers. Sections through the cyst wall itself showed uneven thickening of the intima and occasional calcified atheromatous plaques in the fibrous connective tissue wall. Only rare bundles of smooth muscle and elastic fibers were seen.

DISCUSSION

Several facts about these and the previously reported cases raise interesting points for discussion and speculation. It seems definite that the lesion is of a congenital character. Goldman,[14] among others, is of this opinion and has emphasized the hereditary nature of this anomaly as well as its frequent coexistence with other visible telangiectases. Yet neither of our patients gave any family history of vascular abnormalities, and neither had other recognizable telangiectases. Several of the patients have not had the usual type of a cavernous hemangioma but have had large cystic aneurysmal structures with which both a branch of the lobar artery and vein communicated. It has not yet been possible to determine whether this is the same type of lesion with the same type of etiology and origin as the cavernous hemangioma. Furthermore, no relationship has been established between the degree of polycythemia and cyanosis and the pathologic type of the lesion.

The effective size of the arteriovenous shunt presumably determines the degree of unsaturation of blood returning to the left heart, the cyanosis, the secondary polycythemia, the increased blood volume, increased cell volume, and the increase in the hemoglobin content of the blood. Yet our first patient with a lesion quite similar to the second, did not have these associated changes in the peripheral blood. The explanation that the effective size of the shunt in her was not sufficient to cause them does not seem adequate since there were direct communications between the sac and the pulmonary arteries and vein. The character of the bronchial artery found at operation, and its apparent anastomosis with the sac may be significant. We are unable to say whether this connection with the sac was a direct one or through the pulmonary capillary system, yet it is possible that this association may have been a factor in explaining the absence of the expected blood changes. Maier and associates[12] have suggested that the bronchial arteries may play a role in supplying blood to a fistula, but as far as we are aware the evidence for this concept has not been as clear in any of the other reported cases as it was in this one.

The occasional mistaken diagnosis of polycythemia vera in the early reports, and the use of therapeutic measures for that disease is understandable. However, a patient with a pulmonary tumor visible by x-ray examination, who has an audible bruit, cyanosis, and clubbing of the fingers and whose blood studies show polycythemia, increased hemoglobin content of the blood and normal platelet and white blood cell counts should be considered to have an arteriovenous fistula in the lung whether or not other signs and symptoms are present. Blood volume and oxygenation studies of the arterial blood offer confirmatory evidence. Other interesting diagnostic aids are the Valsalva and Müller tests. Lindgren[11] has emphasized their importance and the fluoroscopic changes in the sacs when they are applied.

The deaths of some patients from pulmonary hemorrhage and other complications such as hemoptysis and symptoms of mild cardiac failure indicate the danger from the abnormality. Surgical resection is the indicated treatment and should be performed wherever possible.

SUMMARY

Two cases of arteriovenous fistula of the lung which were surgically resected are reported.

The signs, symptoms, and diagnostic criteria of this anomaly are discussed.

One patient did not have the polycythemia and associated blood changes usually observed in this abnormality. It is suggested that a connection between the bronchial artery and the aneurysmal sac may offer the explanation for this fact.

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THE PREVENTION OF SPREAD DURING PULMONARY RESECTION BY THE USE OF A DOUBLE-LUMEN CATHETER*

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SINCE the introduction of chemotherapy and antibiotics in combination with postural drainage it has been possible to reduce the amount of sputum to practically nothing in many cases with suppurative pulmonary disease before the operation. There are, however, cases of longstanding saccular bronchiectasis, chronic lung abscess, secondary suppuration behind a bronchiogenic carcinoma, and pulmonary tuberculosis, in which the amount of sputum is reduced by prolonged preoperative treatment but still remains at a considerable level. And *there are cases which seem to be completely dry, and yet pressure on the diseased* portion of the lung during the operation will result in flooding of purulent material. In a group of 125 cases of pulmonary resections from 1937 to 1947, Moody found spreads in 21.7 per cent with 5 deaths due to the spread.

An active control of the secretion during the removal of the infected part of the lung tissue is therefore necessary. The oldest and most commonly used method for that purpose is repeated tracheobronchial aspirations by catheter. This method alone is, however, not entirely satisfactory. The danger of spread is probably considerably decreased with the prone positioning of the patient during the operation as advocated by Overholt. This is brought about by gravity drainage of the secretions and the preservation of the cough reflex through the use of local anesthesia, but the danger of spread still exists.

Still there is a need for some mechanical device which will prevent the flooding of unaffected lobes with pus or blood from sudden hemorrhage during the operation. *Such instruments have been constructed according to two different* principles:

1. The healthy lung has been separated from the diseased by the use of an endobronchial anesthetic tube with an inflatable rubber cuff (Gale and Waters, 1931, and Magill, 1936).

2. The main bronchus to the diseased lung has been occluded (Crafoord, 1938, Halton, 1943, and Moody, 1947, 1948, and 1949). These different methods are reviewed by Moody, 1948 and 1949.

At the Sabbatsberg Hospital in Stockholm, the Crafoord technique of bronchial tamponade has been used in about 500 cases and has on the whole proved satisfactory in most cases. But there have been cases in which the tamponade has slipped out of place and obstructed both main bronchi, and it had to be removed quickly. When ideally applied, the tamponade should permit gas exchange but not allow the secretions to pass through. If the tamponade is too firmly packed or has been moistened by the secretions, the gas exchange to

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*The catheter described in this paper was made by Trelleborgs Gummifabrik, Trelleborg, Sweden, and is obtainable from A. B. Stille-Werner, Stockholm 4, Sweden.

the diseased area will be diminished to a minimum and be of no value in oxygenating the patient. It is sometimes difficult to compress the lung, since the gas remains behind the tamponade and keeps the lung distended to such a degree that it hinders the surgeon.

Both these disadvantages are avoided with the endobronchial balloon devised by Moody. The bronchus to the diseased lung is obstructed by a balloon encased by a metal holding apparatus with numerous protruding small points. The latter are embedded in the bronchial wall by inflation of the balloon, preventing its slipping back into the trachea. Suction can be applied through and distal to the balloon and atelectasis of the portion of the lung to be resected can therefore be achieved. Bronchoscopy is necessary for introduction of the balloon. An ordinary endotracheal tube is then inserted. In a series of 44 cases, Moody reported that the balloon slipped out of place in 1 case. There were 6 cases with contralateral spread, 1 of which was fatal. In 33 cases of 44 the instrument was considered to function satisfactorily. The instrument is not applicable in upper lobectomies.

No instrument so far has been devised to prevent the spread of purulent secretions from the right upper lobe.

THE USE OF THE DOUBLE-LUMEN CATHETER TO PREVENT THE SPREAD OF PURULENT SECRETIONS

In 1949, one of us (E. C.) devised a new flexible double-lumen catheter for bronchospirometry (see Fig. 1).

The catheter is made of rubber of approximately the same rigidity as an ordinary urethral catheter and provided with a small hook that is automatically engaged by the carina. The inner diameter of each lumen is 7 mm. in the catheter for men and 6 mm. in the one for women. The catheter is introduced under topical anesthesia without the aid of fluoroscopy or bronchoscopy. Under mirror guidance it is introduced over a curved metal stylet. The rubber hook is tied down to the catheter with a silk thread until it has been passed through the larynx, when the slipknot is untied. The catheter is then turned 90 degrees to the left and is gently pushed downward. During the introduction it exerts a slight pressure on the left tracheal wall and therefore automatically enters the left main bronchus. It is then easy to feel when the hook is engaged by the carina. Now the cuffs are inflated. Then anesthesia and suction can be applied to each lung separately.

The hook and the two rubber cuffs will maintain the catheter in correct position. It has been used for bronchospirometry in more than 100 cases with satisfactory result. The introduction is easy and the tube is well tolerated even for prolonged examinations during exercise tests.

Since November, 1949, the double-lumen catheter has been used in 20 cases of pulmonary resection. The method has been found so satisfactory that its use will be continued.

Most of the advantages of this method were well demonstrated in the first case in which it was used. This case is therefore described in detail to illustrate the technique.

A 53-year-old man had had 15 pneumonias on the right side since 1941. In April, 1949, a 4 by 5 cm. cavity with a fluid level was demonstrated in the posterior segment of the right upper lobe. Tubercle bacilli could never be demonstrated. Bronchoscopy showed an inflammatory reaction and a considerable amount of secretion in the bronchus to the posterior segment of the right upper lobe, but otherwise a normal bronchial tree.

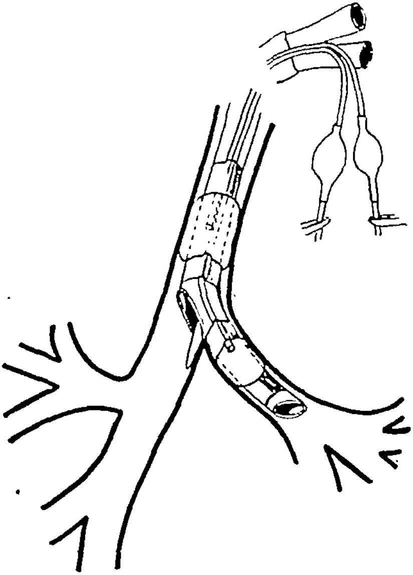

Fig. 1.—Diagram of the double-lumen catheter in position. Notice the small rubber hook that is automatically engaged by the carina.

Intensive medical treatment with penicillin and streptomycin both parenterally and by inhalation as well as sulfonamide therapy was instituted. After seven months of medical treatment, the sputum still remained above 100 ml. per day and the size of the abscess had not diminished. The patient also suffered from a severe asthma and had a pronounced emphysema as shown by the following values of the respiratory function:

Vital capacity	2,330 ml.
Residual capacity	2,440 ml.
Total capacity	4,770 ml.

The residual capacity was as much as 51.2 per cent of the total capacity (normal value 23± 2.5 per cent).

The Operation.—After topical anesthesia with 2 per cent Pantocain in pharynx, larynx, trachea, and the main bronchi, the double-lumen catheter was introduced and both lumina connected with the anesthesia apparatus. General anesthesia was induced with pentothal and continued with nitrous oxide, oxygen, and curare (see Fig. 2).

The right side of the chest was entered through the bed of the sixth rib. From this time controlled respiration was maintained to the left lung only by the use of the spiro-

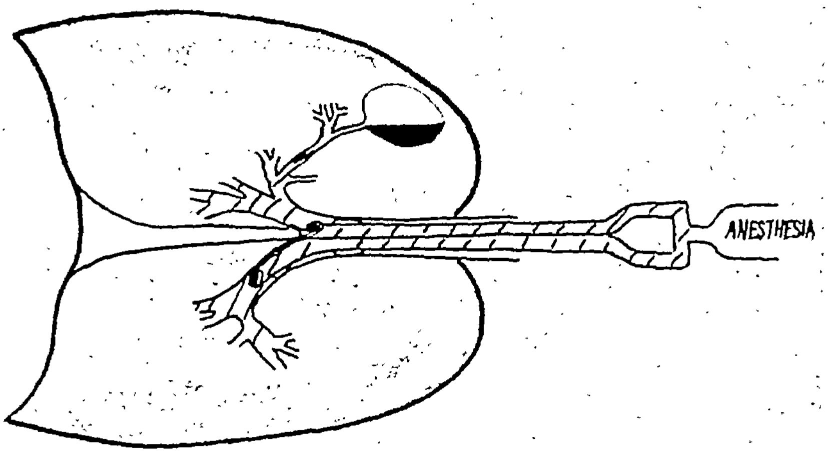

Fig. 2.

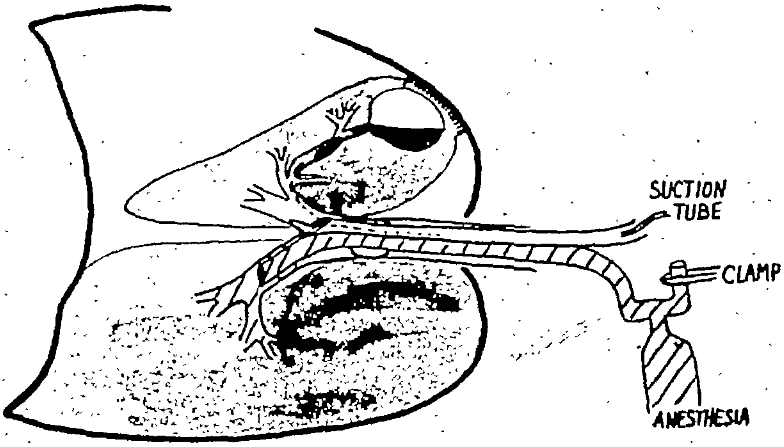

Fig. 3.

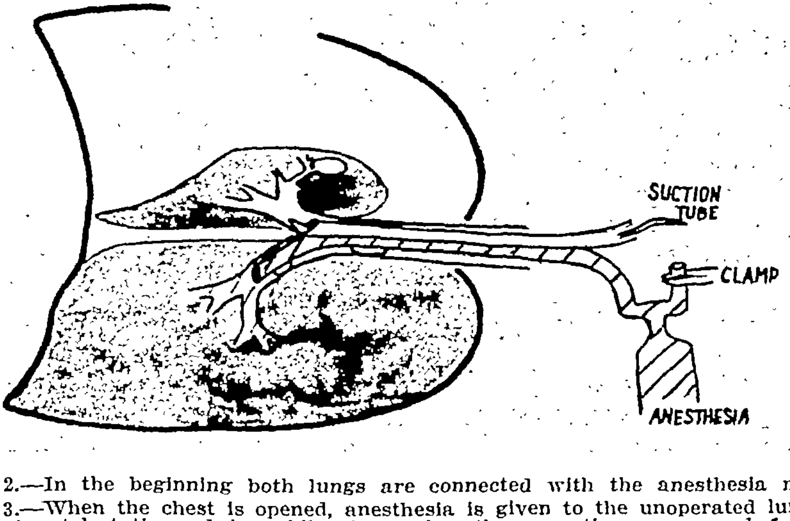

Fig. 4.

Fig. 2.—In the beginning both lungs are connected with the anesthesia machine.

Fig. 3.—When the chest is opened, anesthesia is given to the unoperated lung only. The right lung is atelectatic and immobile, increasing the operating space and facilitating the separation of the lung from the chest wall. Continuous suction is applied in the right bronchi.

Fig. 4.—After separation of the lung from the chest wall the dissection of an incomplete fissure was found difficult on an atelectatic lung.

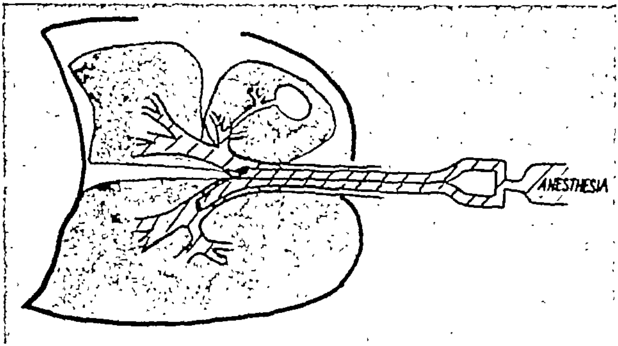

Fig. 5.

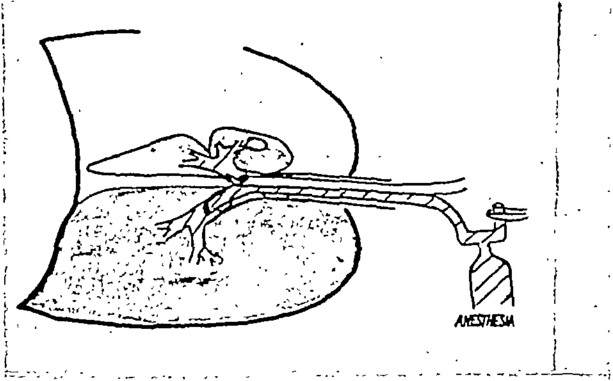

Fig. 6.

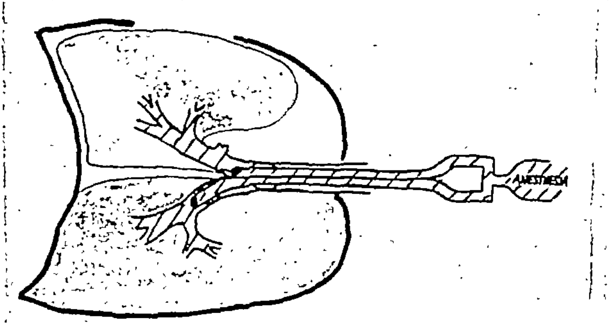

Fig. 7.

Fig. 5.—Both lungs are connected with the anesthesia machine. The separation of lobes in the fissure was facilitated by the inflation of the lung.

Fig. 6.—The left lung only is connected with the anesthesia machine when dissection of hilum is carried out.

Fig. 7.—After completion of the right upper lobectomy the anesthesia was continued on both lungs.

pulsator. The tube to the right lung was disconnected and left open. The right lung then became atelectatic and was held out only by dense adhesions over the diseased area (see Fig. 3).

Thus, more operating space was obtained in the right chest, facilitating the separation of the lung from the chest wall, which had to be done in the extrapleural plane. During the handling of the abscess-containing area, a copious amount of purulent material emptied out into the major bronchi and was removed by continuous suction with a plastic tube introduced through the open right lumen of the double-lumen catheter. During this procedure the right lung did not move at all, which furthermore contributed to the prevention of spread.

When the lung had been completely separated from the chest wall, the dissection of an incomplete fissure between the lobes was found difficult on an atelectatic lung (see Fig. 4). Therefore, when all secretion had been aspirated from the bronchial tree, the right lumen of the catheter was connected with the anesthesia machine. The right lung was thus inflated, facilitating the separation of the upper lobe from the middle and lower lobes in the fissure (see Fig. 5).

Then again, the right tube was opened, rendering the lung atelectatic during the dissection and division of the vessels and the bronchus (see Fig. 6). It was now found that the patient had such a decreased pulmonary reserve, that prolonged one-lung anesthesia produced a pronounced cyanosis. The right lung was therefore inflated for short periods at intervals, which diminished the cyanosis.

When the right upper lobe lobectomy was completed, the anesthesia was continued on both lungs (see Fig. 7).

The double-lumen catheter remained in place for six and one-half hours. The patient recovered and the result is considered satisfactory.

There were 2 cases with right upper lobe suppuration behind bronchiogenic squamous-cell carcinomas. Left-lung anesthesia was continued throughout the operations. The right lungs were atelectatic, which greatly facilitated the division of adhesions and the extrapleural separation of the diseased lung tissues from the chest wall. Although one of the patients had no sputum before the operation, a considerable amount of purulent material was aspirated through the right part of the double-lumen catheter during the operation.

When the bronchus is ready for division and the bronchial tree is dry, the catheter is pulled out 1 cm. for right side pneumonectomies and 5 cm. for left side pneumonectomies to avoid injuring the catheter when the clamp is applied to the bronchus.

The anesthesia is then continued to the remaining lung through both lumina of the catheter and only the proximal rubber cuff is inflated.

Seven more pneumonectomies were performed with the technique described, 3 on the left side and 4 on the right side, 6 of them for bronchiogenic carcinoma and 1 for cystic lung disease.

Two more lobectomies were performed with the aid of the double-lumen catheter, 1 right middle lobe lobectomy for tuberculosis and 1 right lower lobe lobectomy for bronchiectasis. In 1 case with a tuberculous cavity in the apical segment of the left lower lobe, a segmental resection was performed. In all cases the result has been satisfactory, the catheter has remained in place and has prevented spilling over of purulent secretion.

Indications.—The method described is recommended in any resection for suppurative pulmonary disease including bronchiectasis, lung abscess, bronchiogenic carcinoma, and adenoma with secondary suppuration and tuberculosis. Arteriovenous aneurysm of the lung with the danger of intrabronchial hemorrhage during the operation is also considered an indication. Also, in enucleation-resection of benign lung tumors, the double-lumen catheter is advocated because of the ease in production of atelectasis of the tumor-containing lung during the enucleation.

Bilateral bronchiectasis is not considered a contraindication. There are often dense adhesions in the diseased area of the lung, which are more easily divided when the lung is atelectatic, and the handling of the bronchiectatic lobe will produce a flooding of purulent secretion which is prevented from entering the other side. Repeated aspirations by a small catheter on both sides is a necessity.

It is true that when the atelectasis is produced, a considerable amount of blood is passing nonventilated lung tissue. Thus, an arterial oxygen deficit will result. In cases with a very low respiratory reserve, this arterial oxygen deficit is sufficient to produce a pronounced cyanosis, as in the first case described. Inflation of the atelectatic lung for short periods at intervals is then necessary.

SUMMARY

The double-lumen catheter has been adopted for the prevention of transbronchial spread during pulmonary resection. One-lung anesthesia with atelectasis of the lung to be operated will provide more operating space and facilitate the separation of the lung from the chest wall. Furthermore, there will be less movements of the diseased part of the lung, which will contribute to diminish the danger of spread.

Continuous suction can be applied to the bronchus draining the diseased area. The lung can be inflated when desired.

The method has proved satisfactory and is considered to be the best way to prevent spilling over of purulent secretions or blood from a sudden hemorrhage. It is the only method that can be applied in cases with suppurative disease in the right upper lobe.

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CONSIDERABLE IMPROVEMENT FOLLOWING EXPLORATORY THORACOTOMY IN TWO CASES OF TETRALOGY OF FALLOT

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THE Blalock operation has been performed by us for twelve patients having the tetralogy of Fallot, with one death. In two other patients an anastomosis could not be accomplished; extensive vascular pleural adhesions were divided and considerable dissection was carried out in the mediastinum; both these patients attained a large measure of improvement as to the signs and symptoms of their disease. The three operations in these two patients were easily borne. The improvement in the patient who had two operations was similar to that following a successful anastomosis, although it took a little longer to complete itself.

CASE REPORTS

Case 1.—C. B., born on June 6, 1934. The parents first noticed dyspnea, cyanosis, chilliness, polydipsia, and occasional fainting when the patient was 6 months of age. The mother had had no infectious disease or trauma during pregnancy, and delivery was on time and normal.

Preoperative examination, Dec. 9, 1948, was of a 14-year-old child of normal physical and psychic development. A systolic murmur was heard parasternally in the left second intercostal space and the liver was enlarged. An excess of salts and bile pigments were present in the urine. The x-ray film showed enlargement of the right auricle, a slightly concave pulmonary conus, and an aorta descending on the left side. In the left anterior oblique position, the subaortic window was clear.

With angiocardiography the pulmonary artery was best filled during the fifth second. There was apparently a stenosis of the main pulmonary artery and a relative dilatation distal to the stenosis. The left auricle and ventricle were opaque only during the ninth second.

The ocular fundi were normal except for slight venous dilatation. The blood count showed red blood cells, 5,020,000 and white blood cells, 3,800. The oxygen saturation of the arterial blood was 69 per cent (Haldane's method); the sedimentation rate was 7 mm. in twenty-four hours, which is low.

Operation, right anterior approach, was on Dec. 14, 1948. Seventy minutes were needed to divide extensive vascular adhesions between the lung and upper mediastinum and to free the right pulmonary artery, which was of normal size and not pulsating. Ten cubic centimeters of 1 per cent procaine solution were injected into the superior mediastinum. The azygos vein was divided and the innominate artery was being sought when the systolic blood pressure dropped from 105 mm. Hg to 70 mm. and the pulse rate was uncountably fast. The lung was then inflated and more procaine injected into the mediastinum. The blood pressure rose and the pulse rate dropped. Resumption of the operation caused a second and, later, a third repetition of the unfavorable events and, therefore, the surgeon, internist, and anesthetist agreed that the operation should be ended.

The only unfavorable postoperative events were an apyretic jaundice of two weeks' duration and syncope on two occasions. Ten months after operation a striking improvement

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was noted in the patient's height and weight; cyanosis was seen only after exertion; dyspnea was much less and the child walked and ran like a "blue baby" whose operation had been a success. He had no more fainting attacks and he was serving as a carpenter's apprentice. Examination of the heart showed no change from the preoperative condition; the pulse was 120, and the liver was slightly enlarged. The blood count showed on Oct. 12, 1949, red blood cells, 4,270,000. The oxygen saturation was 87 per cent.

In brief, ten months after an operation in which many vascular pleural adhesions were divided, and in which dissection within the mediastinum was carried out, but in which no vessel anastomosis was accomplished, the patient's condition improved as much as would have been expected if an anastomosis had been performed.

CASE 2.—G. C., born in 1935. Cyanosis and slight dyspnea, which increased with crying and exertion, appeared fifteen days after birth.

Preoperative examination, Oct. 13, 1948, was of a 13-year-old boy of small size but otherwise of normal development. There was severe cyanosis and clubbing. Dyspnea was slight at rest but increased with exertion, even on talking. Running was followed by fainting. A systolic murmur was heard parasternally in the left second intercostal space. The pulse rate was 65 and the blood pressure 110/60. The x-ray film showed a concave left pulmonary conus, an aorta descending on the right side, and in the left anterior oblique projection, a clear subaortic window. The hila and the pulmonary fields were not abnormally clear.

The electrocardiograms showed bradycardia, good voltage, and right axis deviation. The oxyhemoglobin saturation was 51 per cent and the total capacity of blood in oxygen, 17 c.c., or 7 per cent. The sedimentation rate was 1 mm. in twenty-four hours. The blood complement fixation test was negative for syphilis.

The first operation was performed on Oct. 8, 1948, through a *left* anterior incision. The pleural cavity was practically obliterated by uniform, short, cylindrical cords. On sectioning them, each was found to consist of a blood vessel, which bled dark blood more *actively from their parietal rather than from their pulmonary ends; these* many vessels obviously constituted important arterial pathways from the general circulation to the lung. The pulmonary artery was surrounded by an extensive network of fragile vessels which also fed the lung from the general circulation. Seventy-five minutes were needed to free the pulmonary artery to the pericardium; the artery did not pulsate. A superior left vena cava passed behind the left pulmonary artery. After a search of an hour, an innominate trunk was found dividing into carotid and subclavian trunks and a third branch passing downward and mesially; this trunk was wide at its origin and then became progressively narrower and its termination could not be identified; it was too narrow and its wall too thin for use in an anastomosis; it had the appearance of the abnormal vessel shown in Fig. 27 of Blalock's article in the October, 1948, issue of *Surgery, Gynecology and Obstetrics.* The pulmonary artery was deep and could not be adequately mobilized because of the extensive pleural symphysis; this fixation of the lung prevented the elevation of the lung which is often so useful in the making of an anastomosis without undue tension.

The postoperative course was simple. A pleural effusion was aspirated. Cyanosis and fatigability were more pronounced.

On Jan. 5, 1949, approximately three months after the first operation, an operation was performed on the opposite or *right* side. There were fewer pleural adhesions than on the left side and the pulmonary artery was easier to dissect. Another innominate artery was found on the right side. Even after the carotid and vertebral arteries had been divided and the subclavian artery divided at the origin of its thyrobicervicoscapular branch, the subclavian artery was too short to reach the pulmonary artery, which was abnormally low and could not be mobilized. Even after traction, only 5 mm. of the main trunk of the pulmonary artery, which did not pulsate, existed between its origin and its upper lobe branch. An end-to-end anastomosis would have been impossible.

The anatomic abnormalities encountered could not have been foreseen before operation or, at least, they could not have been accurately judged as insuperable. Angiocardiography does indicate the distance between the subclavian and pulmonary arteries but it does not exclude a successful anastomosis even if the distance is great, provided that there is a long systemic artery or that the pulmonary artery is long and can be mobilized with mobilization of the lung.

A Pott's type of operation might have been used as a second operation on the left side but, having proceeded as far as we did in the hope and expectation of accomplishing an anastomosis, we doubted whether it would have been feasible to perform a Pott's operation through an anterior approach. To have undertaken an arterial graft would have required, in our opinion, an unjustifiable extension of the duration of the operation.

The postoperative course in the second patient was also simple. When the patient was seen as an outpatient in May and October, 1949, a definite, gradual improvement was noticed. Cyanosis was less severe and dyspnea was considerably lessened. The child was able to run and had no more attacks of fainting.

The values for certain laboratory tests before, between, and after the operations showed an important improvement in the oxygenation of the blood and are presented for comparison, as follows:

Red blood cells, before operations, 7,140,000; after operations, 5,300,000.

Oxygen saturation, before operations, 51 per cent; between operations, 59.5 per cent; after operations, 76 per cent.

Many laboratory tests were made. They indicated considerable improvement of all respiratory, circulatory, and tissue functions.

Two hypotheses may be offered to explain the improvement in these two patients in whom no anastomosis could be accomplished, but with a full realization of the fact that two cases are too few and a follow-up period of only one year is too short for valid hypotheses or conclusions:

1. The probable creation by surgical trauma of new vascular adhesions in the pleurae and mediastinum which may be functioning as many little "ducti arteriosi."

2. A sympathetic vasomotor effect on the pulmonary circulation as a result of prolonged dissection in the region of the right subclavian artery. In both cases, improvement or disappearance of the attacks of syncope occurred after operation.

SUMMARY

Two cases of the tetralogy of Fallot are reported in which a surgical anastomosis between the systemic and pulmonary vascular systems could not be accomplished. Great improvement followed exploratory thoracotomy with extensive dissection of pleural adhesions, the mediastinum, and pulmonary hilum. The possible mechanism of the improvement is discussed.

RESECTION OF TRANSVERSE PROCESSES IN PULMONARY TUBERCULOSIS

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THE removal of the transverse processes of the vertebrae was first suggested by Friedrich in 1914. Since then, many changes have occurred in the treatment of pulmonary tuberculosis by thoracoplastic procedures. More attention is given now to the obliteration of cavities, to a more complete collapse of the involved lung, and to a greater conservation of uninvolved lung.

Even though there has been a rapid growth in the use of surgery in pulmonary tuberculosis, surgical removal of the vertebral transverse processes in this form of tuberculosis is still a subject of controversy. It is the purpose of this paper to discuss the factors to be considered in determining the value of the removal of the transverse processes in the collapse therapy program and to describe an effective technique of removal.

Improvements in the technique of thoracoplasty during recent years have more than doubled the percentage of patients whose tuberculous pulmonary cavities have been closed completely. This is an actual increase in the percentage of success, and not just the exclusion of poor risk cases, resulting from the division of the modern muscle splitting operation into multiple small stages which made it possible to apply thoracoplasty to many patients who could not have withstood a one- or two-stage classical operation.

Notwithstanding the introduction of newer surgical methods and the removal of longer rib sections, if the transverse processes were not removed, apical cavities often were not closed. If one considers the anatomy of the chest (Figs. 1, 2, and 3) and realizes that the bodies of the vertebrae project into the chest cavity and the transverse processes of the vertebrae and the attached ribs come out rather far, it can easily be understood that even though the rib is removed back to the transverse process there is still part of the lung in the vertebral gutter which is not compressed. In those cases in which the entire head and neck of the rib are removed the remaining outstretched transverse process acts as a sheltering arm to prevent complete obliteration of the costovertebral space.

The routine removal of the entire lengths of the vertebral transverse process and the underlying neck and head of the rib at, and somewhat above and below, the level of the pulmonary cavity or cavities greatly increases pulmonary collapse by *obliterating the costovertebral space*. In those cases in which the transverse processes are not removed, the stumps support the lateral reformed chest wall, holding it out beyond the vertebral bodies to such an extent that the vertebral gutter is usually left and the collapsed lung is safely lodged (Fig. 4, *a* through *e*). A certain amount of movement of the lung is still possible.

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Hence, a posterior cavity remains open, even if only a slit, and a cavity that has been posteriorly displaced by the collapse will be protected and fail to close in. Complete collapse and efficient closure of the cavity are, therefore, usually not possible without the obliteration of this space.

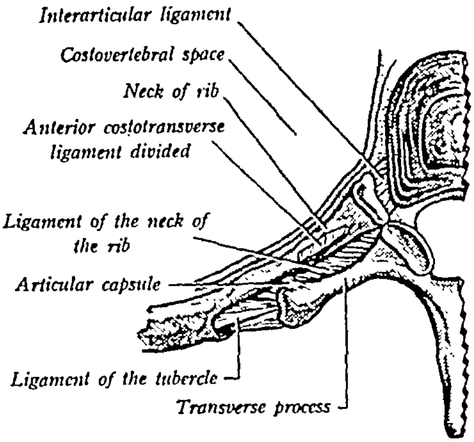

Fig. 1.—Diagrammatic drawing showing the normal anatomy of the costotransverse and costovertebral articulations viewed from above.

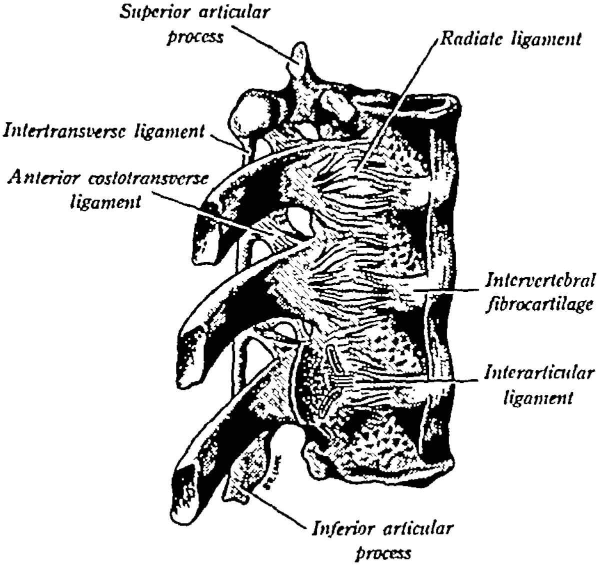
Superior articular process
Radiate ligament
Intertransverse ligament
Anterior costotransverse ligament
Intervertebral fibrocartilage
Interarticular ligament
Inferior articular process

Fig. 2.—Diagrammatic drawing showing the normal costovertebral articulation viewed from the right. After Spalteholz's "Hand Atlas of Human Anatomy," Philadelphia, J. B. Lippincott Company.

The following technique has been found effective in insuring proper and adequate removal of the head and neck of the rib and the transverse process. The desired segment of the rib is removed as far back as one inch from the tip of the transverse process. The periosteum is stripped from the outer surface of the rib to the tip of the transverse process and on the inner surface from the neck and head of the rib. The sacrospinalis, semispinalis, and multifidus muscles lying over the transverse processes are mobilized and retracted mesially, widely exposing the articulation of the rib with the transverse process (Fig. 5). The index finger is introduced between the neck of the rib and the periosteum that has been separated from it. With a gentle milking motion the periosteum is pushed forward as much as possible so as to protect the underlying pleura from future injury. With the palpating finger one is able to feel the groove marking the articulation of the transverse process with the rib. A scalpel with a one-inch blade is inserted into the groove, parallel to the transverse process and dividing the ligament of the tubercle. A scalpel with a nondetachable blade has been found to be more satisfactory than one with a detachable blade because of the occasional breaking of the latter. A Kinsella elevator is then inserted into this opening and with a gentle rocking motion, while the free end of the rib is pushed forward, the articular capsule, the anterior and posterior costotransverse ligaments on the superior surface of the neck of the rib, and the ligament of the neck of the rib are divided in the order given. The rib may now be pried forward with the thumb or a curved periosteal elevator. This maneuver is intended to tear the interarticular and radiate ligaments, and the articular capsule. No attempt is made to cut these structures because of the great danger of damaging one of the larger vessels in this area. The rib is now firmly grasped with a bone holder as near to the head of the rib as possible and twisted back and forth so as to sever any remaining strands of the interarticular and radiate ligaments, and the articular capsule. Thus, the head and neck of the rib are removed completely by disarticulation. It should be noted that failure to grasp the rib properly will cause the rib to break, with the result that the head and part of the neck will be left behind. If the procedure is performed properly, the neck and head of the rib are removed in one piece and the head has a shiny, smooth, white appearance.

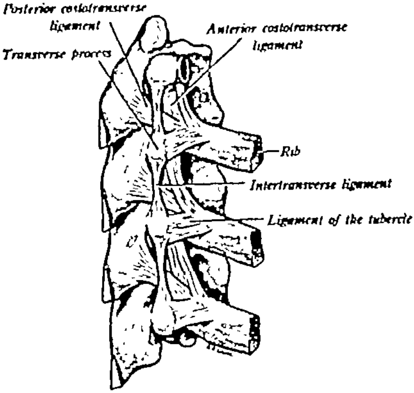

Fig. 3.—Diagrammatic drawing showing the normal costotransverse articulation viewed from behind and somewhat from the right. After Spalteholz's "Hand Atlas of Human Anatomy," Philadelphia, J. B. Lippincott Company.

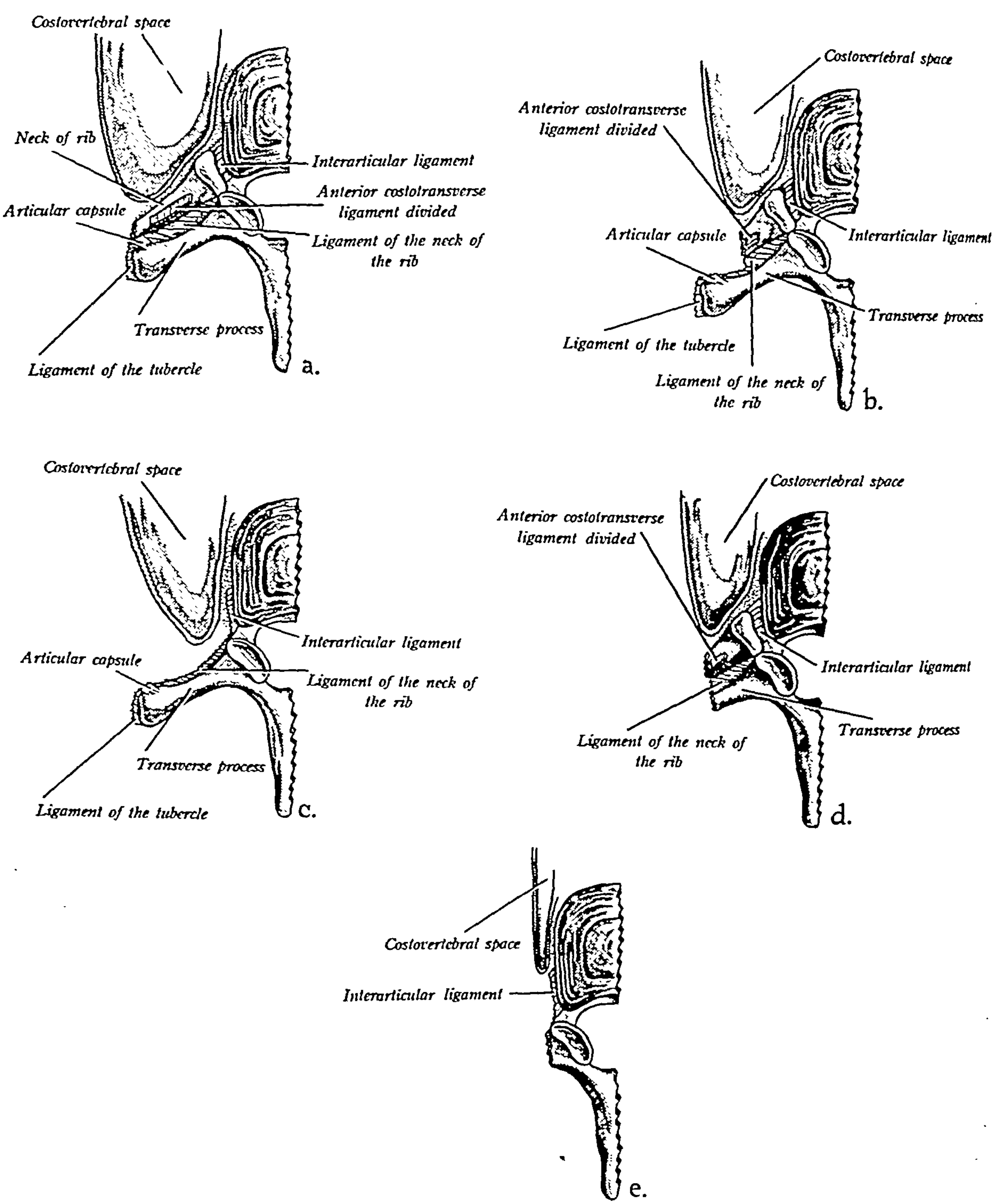

Fig. 4.—*a* through *e*.—*a*, Diagrammatic drawing showing the incomplete obliteration of the costovertebral space from failure to remove the head and neck of the rib and the transverse process.

b, The head and a small part of the rib remain. The transverse process acts as a sheltering arm preventing collapse of the costovertebral space.

c, The entire rib has been removed but the transverse process still prevents obliteration of the costovertebral space.

d, Portions of the rib and transverse process remain preventing adequate closure of the costovertebral space.

e, The entire rib and the transverse process have been removed allowing the costovertebral space to fall in and become obliterated.

The transverse process is now exposed. The levator costarum and the rotatores muscles are stripped from the end and the upper and back part of the transverse process. The intertransverse ligaments are divided on each side of the transverse process. Then the attachments of the anterior and posterior costotransverse ligaments on the transverse process are divided, completely isolating the transverse process, which will be found to be approximately 2 cm. long. With one or two bites of the Sauerbruch's square-nosed rongeurs, all of the transverse process is removed almost flush with the pedicle of the vertebra.

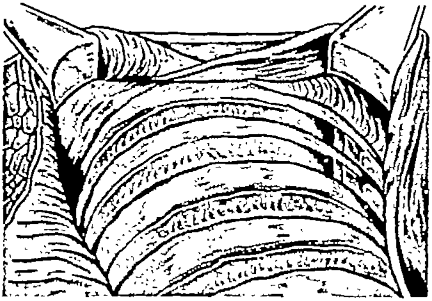

Fig. 5.—Diagrammatic drawing showing the sacrospinalis, semispinalis, and multifidus muscles lying over the transverse process mobilized and retracted mesially, widely exposing the costotransverse articulations.

At times it is not necessary to resect the first vertebral transverse process. However, caution must always be taken in handling this transverse process, since the first thoracic nerve may easily be injured. Also, it is not necessary to resect the second vertebral transverse process as much as the transverse processes below. In those cases in which the apex of the lung drops, the upper two transverse processes rarely interfere with the closing of cavities. This situation is much to be desired because the operative time in resecting the upper two ribs is lessened, the lateral support of the vertebral column in this region is not weakened, and there is no danger of damage to the important nerve structures near the first rib. If the apex does not drop, then it is necessary to remove completely the first two transverse processes to insure maximum collapse in this area.

SUMMARY AND CONCLUSION

In summary it can be said that resection of the vertebral transverse processes in the treatment of pulmonary tuberculosis is favored because complete collapse and efficient closure are thereby possible. The technique presented has been found effective in closing cavities with a minimum of damage to important structures.

LUNG-PLEURA GRAFT FOR ESOPHAGOESOPHAGEAL ANASTOMOSIS

An Experimental Study

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TWO esophageal anastomoses were recently performed for benign congenital stricture of the lower third of the esophagus. One healed primarily, the other developed a leak at the suture line. The latter healed satisfactorily without stricture, but only after a greatly prolonged hospital course. The difficulty in primary healing in isoesophageal anastomosis has long been recognized, and has been attributed[1-4] to a multiplicity of alleged factors, most of which are absent or minimal in healing of the remainder of the gastrointestinal tract. Such factors include (1) scanty blood supply, (2) lack of a true serosal coat, (3) tension on the suture line following resection, (4) variation in tension on the esophagus with each diaphragmatic excursion, (5) inability to put the esophagus at rest by control of deglutition, (6) poor conditions for accomplishing a satisfactory anastomosis due to the anatomic position of the esophagus, (7) danger of postoperative infection—mediastinitis, esophagitis, empyema, pneumonia, (8) danger of shock and/or cardiac arrest from interference with the vagi, (9) lack of an omentum to protect and favor healing of the suture line, (10) postoperative pneumothorax, (11) postoperative hemorrhage, (12) postoperative diaphragmatic hernia, (13) inanition, and (14) postoperative chylothorax. The presence in the literature of reports of many successful esophagogastrostomies,[5, 12] and several esophagoesophageal anastomoses,[4, 13, 14, 15] indicates that these factors are not unsurmountable. However, any procedure that might diminish the part such factors may play in the eventual outcome of the operation should be investigated. In intestinal surgery the anastomotic line is frequently reinforced with omentum, either as a pedicle graft or a free transplant, to prevent leakage. It seems reasonable to expect that the same type of procedure might be beneficial in esophagoesophageal anastomosis. Therefore, a series of experiments was performed in dogs to test the applicability of reinforcing the suture line in esophagoesophageal anastomosis.

EXPERIMENTS

Adult mongrel dogs were used. An esophagoesophageal anastomosis was made in each dog. A simple continuous suture of 000 chromic gut was used for the mucosal stitch, and a simple interrupted suture, of the same material, was used for the muscular layer. The technique was precisely the same as reported in previous studies from this laboratory.[16] Following completion of the anastomosis, a triangular portion of the lower edge of the left lower lobe of the lung was excised. A rubber-shod noncrushing clamp was applied proximally for control of hemorrhage, and to facilitate repair. Interrupted overlapping figure-of-eight su-

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tures of 00000 plain gut were used to close the defect in the lung. The section of lung obtained was split lengthwise, so that the piece to be used as a graft was extremely thin, measuring approximately 6 by 1 by .05 cm. Pleura was present on one side, and raw lung substance present on the other side. The graft was placed over the suture line, under moderate tension, with the raw surface against the esophagus, and then sutured. Interrupted sutures of 00000 plain gut were placed through the graft and into the esophageal wall to prevent the graft from slipping. The thoracic cavity was then irrigated with saline, the lung expanded, and closure accomplished in layers with interrupted cotton sutures. A liquid diet was given the first postoperative day, soft diet from the second through the fifth day, and kennel rations thereafter. No antibiotics or intravenous fluid was administered. At specifically designated intervals the dogs were operated on again to study the healing process. When the thorax was opened the amount of infection, extent of the adhesions, appearance of the graft, and condition of the donor area were noted. The grafted area, with a segment of normal esophagus proximally and distally, was then excised and split longitudinally, to afford evaluation of the mucosal healing. Subsequently, microscopic sections, taken at right angles to the suture line, were made to study the cellular reaction.

RESULTS

Nine dogs were used in the experiments. They were equally divided into three groups, with the intervals between the first and second operations varying as follows: Group 1, seven days; Group 2, fourteen days; Group 3, twenty-eight days. The mortality was zero; the morbidity was slight, with each dog, on the average, losing only 300 Gm. between operations. In every case the graft was viable, and adherent to the esophagus. There were less pleural adhesions around the area of the anastomosis than were found in previous experiments, where no lung graft was used. There were no cases of empyema; the donor site healed primarily in every case. In all cases the mucosa showed healing without any evidence of leak or infection. The gut sutures were still present in the seven-day group, but not in the other two groups. Microscopically, beginning vascularization was seen in each case; the degree varied with the time interval. Less inflammatory reaction was observed microscopically than had been noted when grafts were not used. There were no focal accumulations of polymorphonucleocytes or lymphocytes to suggest acute or chronic abscess formation.

It has been possible to achieve excellent results experimentally without the use of a graft,[16] but the healing process, with the graft, proceeds at a strikingly more rapid pace. A seven-day grafted anastomosis has the degree of healing that is usually found in a twenty-one-day plain end-to-end anastomosis.

DISCUSSION

Haight,[17] Bigger,[18] and Daniel[19] have, in cases of repair of tracheoesophageal fistula, telescoped the distal segment into the proximal, to afford strength to the anastomotic line. Thus, the upper segment covers the suture line of the lower segment. However, a search of the literature does not reveal any experimental or clinical work concerning the use of pleural grafts, whatever the source might be, as a reinforcement for the suture line in esophagoesophageal anastomoses. An article concerned with the experimental use of free peritoneal grafts to cover intestinal anastomotic suture lines has been published recently.[20]

These experiments show the practicability of the use of a thin free lung graft to cover the suture line in isoesophageal anastomosis. The grafts were easily obtained and prepared, the donor sites healed by primary intention, there were no instances of empyema, hemothorax, leaking from the anastomosis, or sloughing of the grafts.

SUMMARY

Experiments have been performed which apparently show the practicability of the use of a free lung-pleura graft as a buttress and reinforcement for the suture line of esophagoesophageal anastomosis in the dog.

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Original Communications

PRIMARY INTRATHORACIC NEUROGENIC TUMORS

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INTRODUCTION

THE purpose of this paper is to present a clinicopathologic study of 24 cases of primary intrathoracic tumors of nerve origin with special emphasis on the classification and pathologic features of these tumors.

REVIEW OF LITERATURE

In 1944, Kent and associates[1] in a paper entitled "Intrathoracic Neurogenic Tumors" collected 105 cases from the literature and added 21 new cases, 18 of which were acceptable histologically. According to the documentation presented, about 78 of the collected cases were actually primary intrathoracic neurogenic lesions. Twelve (15.3 per cent) of the 78 were *malignant in contrast* to the figure of 37 per cent for the entire series. Of the 18 new cases 41 per cent were classified as malignant. Blades,[2] in 1946, reported 1 neurosarcoma (3.3 per cent) among 30 mediastinal neurogenic tumors. Curreri and Gale[3] stated that 92 per cent of posterior mediastinal tumors are neurogenic and they reported 6 benign and 1 malignant (14.3 per cent) primary nerve tumors in a series of 36 mediastinal tumors. Brewer and Dolley[4] reported 16 benign and 1 malignant neurogenic tumors in a series of 44 mediastinal tumors.

Harrington[5] recorded 51 primary nerve tumors of the posterior mediastinum, of which 5.9 per cent were malignant. Arbuckle[6] reported 11 primary intrathoracic nerve lesions, 2 (18.1 per cent) of which were malignant. Rarely, primary neurogenic lesions are recorded of the anterior mediastinum,[1] lung,[7, 8] diaphragm,[9] and lateral chest wall.[9] Several of the reported cases of medias-

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TABLE 1

CASE	SEX	AGE (YRS.)	SYMPTOMS	LOCATION	GROSS PATHOLOGY	SURGERY		FOLLOW-UP	
					Case of Diffuse Neurilemoma				
1. C. F.	M	22	Hemoptysis, pain	Anterior mediastinum	Tissue for biopsy	2-40	Biopsy		Death from infected, fungating tumor, 1-46
					Cases of Encapsulated Neurilemoma				
2. D. M.	M	26	Asymptomatic	Right upper posterior mediastinum	Encapsulated, firm, 3.5 cm. in diameter; cut surface lobulated, golden yellow to gray	10-42	Total excision	11-45	Asymptomatic, negative x-ray
3. P. S.	M	25	Chronic cough	Left upper posterior mediastinum	Not available; submitted slide	1943	Total excision	9-49	Asymptomatic
4. S. S.	F	36	Asymptomatic	Right lower posterior mediastinum	Encapsulated, cystic tumor with necrotic center, 10 cm. in diameter; lining of soft, brown, friable tissue with yellow areas	4-44	Total excision	7-48	Asymptomatic
5. N. C.	M	50	Fatigue	Right posterior inferior mediastinum	Encapsulated, cystic tumor, 7.5 by 6 by 3 cm. in diameter; on section, two-thirds of tissue composed of blood filled cysts, surrounding tissue soft and yellow brown	6-45	Total excision	9-49	Asthmatic, negative x-ray
6. P. B.	F	31	Pain, right chest for one year	Right upper posterior mediastinum	Encapsulated, firm tumor 3.5 by 5 cm. in diameter; cut surface yellow to gray	9-46	Total excision	9-49	Asymptomatic
7. K. R.	M	25	Cough for one year	Right upper posterolateral chest wall; origin in third intercostal nerve (intrathoracic)	Encapsulated, firm tumor 3 by 2.5 by 2.5 cm.; cut surface homogenously grayish-white	10-46	Total excision	1948	Asymptomatic, negative-x-ray
8. J. S.	M	35	Asymptomatic	Right upper posterior mediastinum	Encapsulated, cystic tumor 4 by 3 by 2 cm.; cut surface composed of two thin-walled, blood-filled cysts	1-47	Total excision	None	

9.	S. L.	M	18	Asymptomatic	Right lower posterior mediastinum	Encapsulated, reddish-brown, 3 by 3.5 by 2 cm.; periphery of cut surface firm, reddish-brown with patulent vessels in center	6-47	Total excision	None	
10.	M. B.	F	57	Dyspnea (left pleural effusion)	Left upper posterior mediastinum	Encapsulated, cystic tumor 15 by 12 by 9 cm.; section showed blood-filled cysts and yellow to gray tissue; some areas appeared necrotic	9-47	Total excision	8-49	Asymptomatic, negative-x-ray
11.	E. F.	F	37	Pain, right shoulder for two years	Right upper posterior chest wall; origin in second intercostal nerve (intrathoracic)	Encapsulated, firm orange-tan, largely solid except for a few small blood-filled cysts. 7 cm. in diameter	4-49	Total excision	None	
12.	C. F.	F	30	Asymptomatic	Left posterior mediastinum	Encapsulated, firm tumor 9 by 7 by 6 cm. weighing 180 grams; cut surface was firm, pale gray, streaked with yellow-orange zones	11-49	Total excision	1-50	Asymptomatic, negative-x-ray
13.	I. B.	F	35	Asymptomatic	Left upper posterior mediastinum	Encapsulated, firm tumor 3 by 2.5 by 1.5 cm.; cut surface firm, bright yellow to gray	3-50	Total excision	4-50	Asymptomatic, negative-x-ray
						Case of Malignant Neurilemoma				
14.	L. G.	F	13	Cough for ten years (diffuse neurilemomatosis)	Right posterior mediastinum	Four encapsulated, hard masses 8 by 7 by 4 cm., 4 by 3 by 2 cm., 2 by 2, and 1 by 2 cm.; cut surface white with yellow streaks and mucoid areas	11-44	Partial excision	7-45 11-45	Local recurrence Death (cachexia)
						Cases of Ganglioneuroma				
15.	A. P.	M	26	Left chest pain for three months	Left upper posterior mediastinum and surrounding subclavian artery	Encapsulated, firm tumor 5 cm. in diameter; cut surface firm, smooth, moist, and light tan	3-45	Excision of thoracic portion; tumor surrounding subclavian artery not removed	7-49	Asymptomatic, negative x-ray; no palpable tumor in neck
16.	T. H.	M	19	Asymptomatic	Right lower posterolateral chest wall (intrathoracic)	No. 1 encapsulated, slightly nodular solid, firm, pearly-white to yellow tumor, 2 by 6 by 13 cm. in diameter	10-46	No. 1, specimen partial excision	1-49	Asymptomatic, negative x-ray

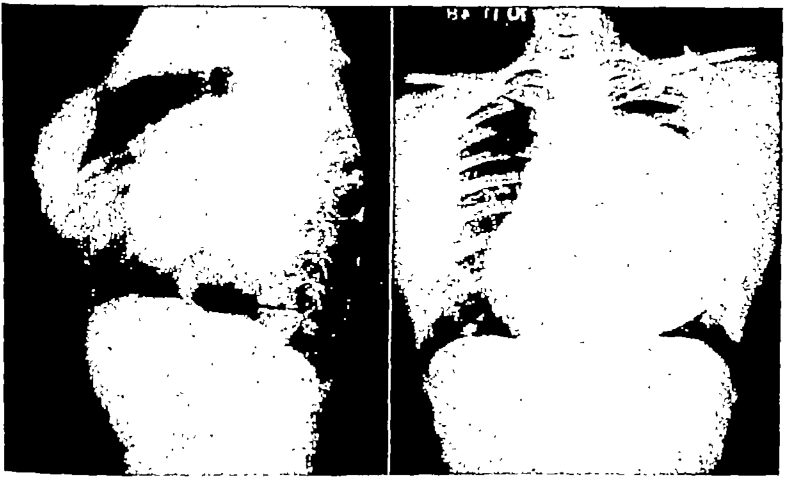
TABLE I—CONT'D

CASE	SEX	AGE (YRS.)	SYMPTOMS	LOCATION	GROSS PATHOLOGY	SURGERY		FOLLOW-UP	
17. R. H.	F	46	Asymptomatic	Right posterior mediastinum	No. 2, encapsulated, firm yellow-gray, translucent, solid tumor 14 by 12 by 4.5 cm. in diameter	4-47	No. 2, specimen total excision of remaining tumor		
					Encapsulated, firm homogenous, glistening, grayish-yellow with attached nerve trunks; 10 by 7 cm. in diameter	11-46	Total excision	1-50	Asymptomatic, negative-x-ray
18. N. F.	F	5	Asymptomatic (café-au-lait spots)	Left and right, upper posterior mediastinum and within left brachial plexus	Tissue for biopsy	5-47	Left thoracotomy, biopsy	1-49	Asymptomatic, x-rays unchanged
19. R. O.	F	6	Cough and dyspnea for one year (identical twin without disease)	Right and left posterior mediastinum	Encapsulated, firm 14 by 10 by 3 cm.; cut surface solid, grayish-white; few attached nerves	7-47	Excision complete except for right intercostal and left posterior mediastinal extensions	9-49 3-50	No recurrence at operative site; no symptoms suggesting progression of residual tumor Asymptomatic except for asthma
20. M. E.	F	14	Dyspnea	Left posterior mediastinum	Three masses together weighing 1,150 grams, incomplete thin capsule; soft, yellow with several attached nerves	11-48	Total excision	5-49	Asymptomatic, x-ray negative
21. J. M.	F	9	Cough	Right and left posterior mediastinum and retroperitoneal	Tissue for biopsy	1-49	Left thoracotomy, biopsy	3-49	Asymptomatic, x-ray unchanged
22. J. H.	F	14	Asymptomatic	Left posterior mediastinum	Encapsulated, soft homogenous, yellowish-gray tumor 2 by 6 by 13 cm. in diameter	8-49	Total excision	1-50	Asymptomatic, negative x-ray
Case of Sympathicoblastoma									
23. J. E.	F	7	Pain, neck mass	Right and left posterior mediastinum	Submitted slide of cervical lymph node	6-48	Cervical lymph node excision	9-48	Skull and pelvic metastases
Case of Paraganglioma									
24. J. H.	M	52	Fatigue, cough (blood pressure normal)	Left upper posterior mediastinum	Encapsulated, soft, red-tan mass 5.5 by 5.5 by 3.5 cm.; cut surface red-gray, soft and homogenous	10-49	Total excision	12-49	Asymptomatic, negative x-ray

tinal xanthomas[10] appear to represent neurogenic tumors (encapsulated neurilemoma) that had a prominent number of lipophages. The number of lipoid-filled histiocytes was marked in several of the tumors in this series.

CLINICAL MATERIAL

The 24 patients on which this report is based include 14 women and 10 men, varying in age from 5 to 57 years (Table I). In 10 instances the lesion was incidentally found during Army separation examinations, tuberculosis surveys, or examinations for other illness. Among the remainder, cough and dyspnea were the most common initial symptoms. Even in the large tumors (Fig. 1, *A* and *B*), pain was not a prominent feature. No instance of "dumbbell tumor" with spinal cord compression was encountered.



A. *B*.

Fig. 1, *A* and *B* (Case 20, M. E.).—Ganglioneuroma showing displacement of the heart but no scoliosis.

The paravertebral gutter is the commonest site for intrathoracic tumors of nerve origin. A diffuse neurilemoma (major component of a teratoma) was encountered in the anterior mediastinum (Case 1) and 2 encapsulated neurilemomas on the inner lateral chest wall. By long usage the paravertebral tumors are considered mediastinal. In this series, 3 ganglioneuromas extended across the anterior surface of the vertebral bodies in the true mediastinum.

The diagnosis of a neurogenic tumor is relatively certain by radiographic examination when a spherical or lobulated shadow is seen in the paravertebral gutter. *The finding of stigmas of diffuse neurilemomatosis (von Recklinghausen's disease)* enhances the diagnosis of a neurogenic tumor. Bone changes consist of widening of intercostal spaces and erosion of adjacent ribs and vertebrae (Fig. 2), due to pressure. There may be enlargement of the vertebral foramina even in the absence of spinal cord signs. Other lesions to be considered are: chondrosarcoma of rib, lipoma,[11] meningocele,[12] aneurysm of descending thoracic aorta, and esophageal achalasia.

Twenty-two patients were operated upon without a fatality. All the encapsulated neurilemomas and the solitary paraganglioma were totally excised, but only 3 of the 8 ganglioneuromas were so treated. Three gang-

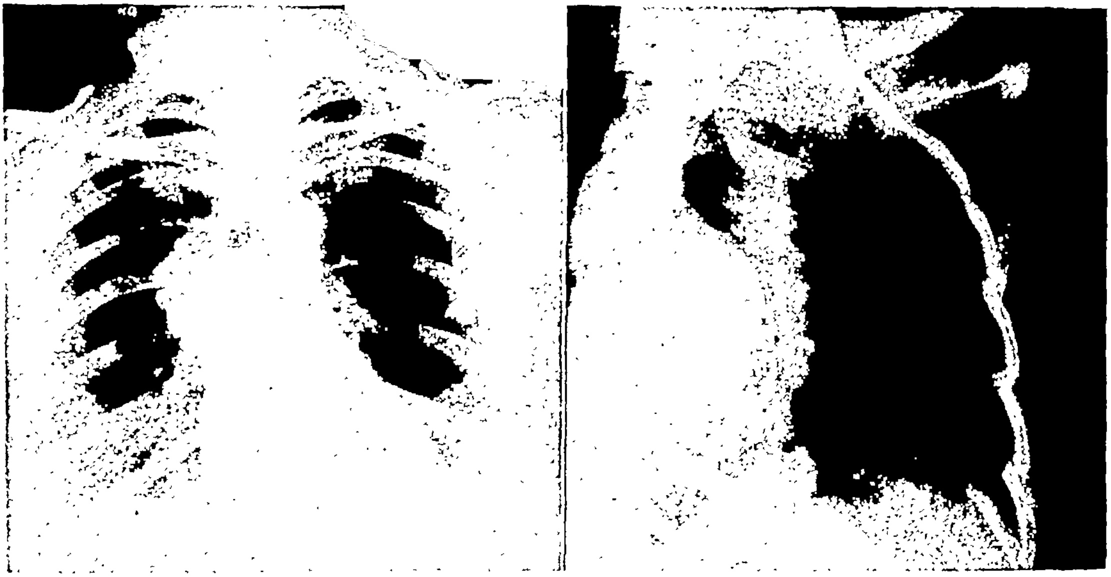

A. *B.*

Fig. 2, *A* and *B* (Case 17, R. H.).—Ganglioneuroma showing separation of ribs and erosion of vertebral bodies.

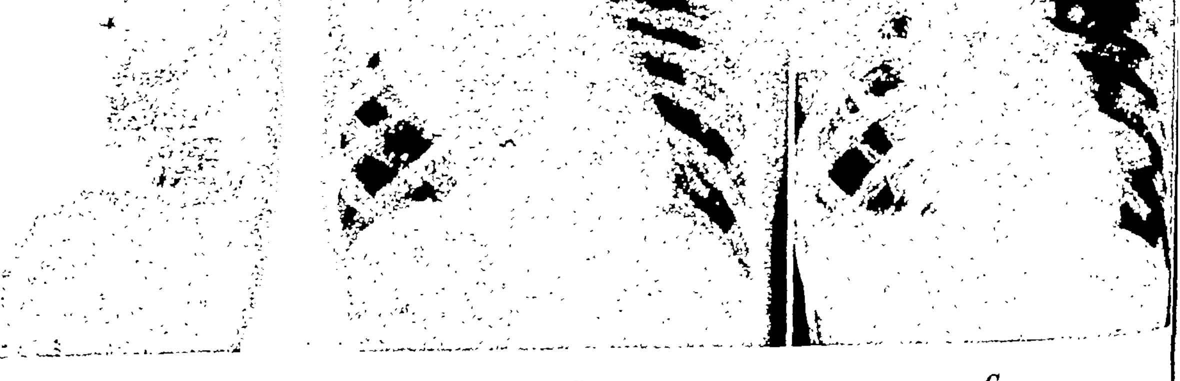

A. *B.* *C.*

Fig. 3.—*A* and *B* show an extensive lobulated malignant neurilemoma. *C* shows postoperative appearance with an apparent metastasis in the right lower lung field.

lioneuromas were subjected to partial excision due to extension of the growth between ribs, along vertebral surfaces, and in one case into the lower neck. The malignant neurilemoma could not be totally removed from the right chest due to encirclement of the trachea (Fig. 3), and only tissue for biopsy was taken from 2 ganglioneuromas, the diffuse neurilemoma, and from a metastatic focus in the case of the sympathicoblastoma.

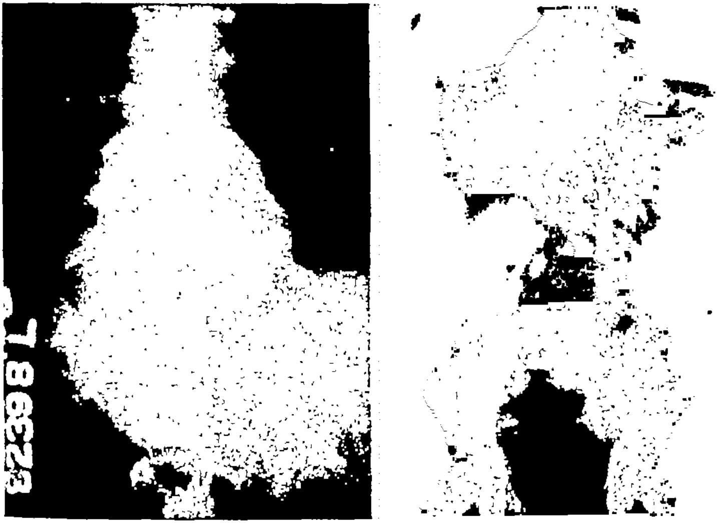


Fig. 4 (Case 21, J. M.).—A fusiform ganglioneuroma displacing the aorta and esophagus to the right.

Surgical technique of extirpation must usually involve a transpleural approach for adequate visualization, preferably through a posterolateral rib bed at the level of the tumor. In children an intercostal incision will avoid scoliosis. The major technical difficulty concerns hemostasis because the branches of the intercostal vessels adhere to the tumor surface, and are present on the side of the growth opposite the operator. Preliminary incision of the parietal pleura completely around the growth and elevation off adjacent ribs will usually allow enough mobility so that the intercostal vessels are stretched and can be visualized crossing vertebral bodies or, on the left, immediately adjacent to the aorta permitting ligation and division under direct visualization. In certain tumors, total removal is impractical due to extension into the neck, across the midline (Fig. 4), or because of sheer bulk; then partial resection is resorted to. No radiographic or clinical evidence of further growth has followed biopsy in 2 instances and partial excision in 3 other ganglioneuromas, the longest now followed over four years (Case 15). Less wide total removal naturally results in failure where one is dealing with a malignant neurogenic tumor. Irradiation does not offer permanent arrest of this tumor.

PATHOLOGY

The tumors included in this study have been classified according to the following scheme, and will be discussed in this order. The number of examples of each is indicated at the right.

I. Tumors of nerve sheath origin	
A. Diffuse neurilemoma[*][†]	1[‡]
B. Encapsulated neurilemoma	12
C. Malignant neurilemoma	1
II. Tumors of sympathetic origin	
A. Ganglioneuroma	8
B. Sympathicoblastoma	1
III. Tumors of paraganglionic tissue	
A. Paraganglioma	1

For a more detailed classification of tumors of peripheral nerves, the reader is referred to a fascicle on the subject by Dr. A. P. Stout, prepared under the auspices of the Armed Forces Institute of Pathology.

TUMORS OF SHEATH ORIGIN

One of the many problems in dealing with tumors of peripheral nerves, and, in particular, the tumors of sheath origin, is their classification. In the laboratories of Memorial Hospital the view has long been held that these tumors are derived from Schwann cells.[14, 15] Nageotte[16] experimentally demonstrated the schwannian origin of the encapsulated neurilemoma in rabbits. Masson and Simard[17] and Masson,[18] stimulated by the work of Nageotte, compared experimentally produced encapsulated neurilemomas with spontaneous encapsulated neurilemomas of man, and were convinced that these tumors were constituted almost exclusively of Schwann cells. This belief has been supported and expanded through tissue culture studies to include the diffuse neurilemoma and malignant neurilemoma.[19, 20, 21, 22]

Stout[23] has suggested that the term "diffuse neurilemoma" be employed *for the tumor commonly called neurofibroma and for the discrete lesion, the* expression "encapsulated neurilemoma." This proposal appears useful to us, because it indicates, on the one hand, histogenetic relationship and, on the other, an anatomic difference. The histologic distinction is certainly not an absolute one, since minor attributes of one lesion may be present in the other, for example, small encapsulated neurilemomas in what is otherwise a diffuse neurilemoma (neurofibroma or plexiform neuroma).

The tumor here designated as diffuse neurilemoma has been most commonly referred to in the past as neurofibroma. Other terms employed include myxoid neurinoma, neurilemoblastoma, neurinoma, plexiform neurinoma, cirsoid neuroma, multiple neurofibromatosis, and von Recklinghausen's disease.

These tumors are seen in most classical form as a manifestation of von Recklinghausen's disease. Characteristically, the lesion may produce beading or diffuse tortuous enlargement of nerve trunks and multiple or solitary nonencapsulated cutaneous tumors.

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[*] Vieta and Pack[13] have employed the term "Plexiform neurilemoma" to indicate the lesion herein described as diffuse neurilemoma.

[†] The designation "schwannoma" may be used synonymously with neurilemoma.

[‡] This tumor was a teratoma growing principally as a diffuse neurilemoma.

Histologically, the tumors are composed of Schwann cells, neurites, and fibrous tissue. The neurites are likely to be scanty.

Metaplasia (cartilage and bone) and more differentiated elements (adult ganglion cells, replicas of Wagner-Meissner tactile corpuscle) may occasionally be noted. The microscopic picture (Fig. 5) may be differentiated from that of the encapsulated neurilemoma by the haphazard arrangement of the Schwann cells, prominent reticulation of the intercellular material, absence of palisading, and other features to be mentioned.

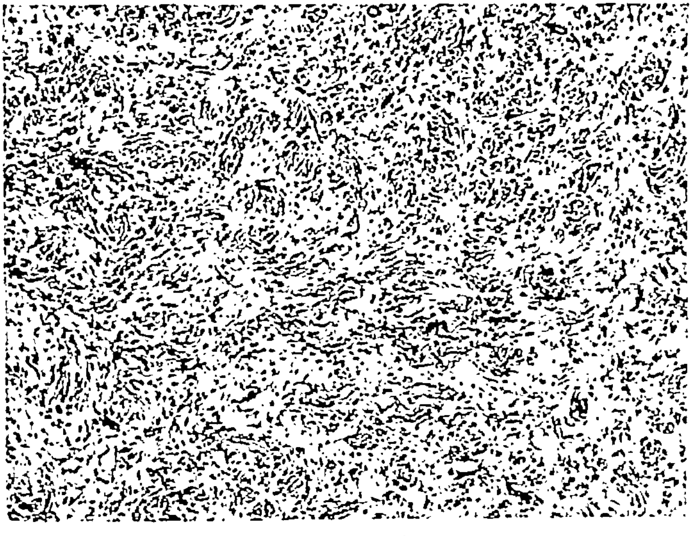


Fig. 5.—Diffuse neurilemoma.

It is important to distinguish the diffuse from the encapsulated neurilemoma because about 13 per cent[24] of diffuse neurilemomas become malignant, whereas encapsulated neurilemomas rarely, if ever, do become malignant. Vieta and Pack[13] are of the opinion that the incidence of malignant change in diffuse neurilemoma is less than 13 per cent. Recently Saxén[25] reported one case which he believed probably represented malignant change in an encapsulated neurilemoma. An occasional case of recurrent or locally infiltrating encapsulated neurilemoma has been reported, as cited by Ehrlich and Martin.[26]

The encapsulated neurilemoma (synonyms: schwannoma, specific nerve sheath tumor, neurinoma, perineural fibroblastoma, peripheral glioma, schwannoglioma, palisaded neurinoma, acoustic neuroma) usually presents as a solitary, encapsulated tumor attached to a nerve from which it may usually be removed without serious damage. Occasionally, however, a tumor is encoun-

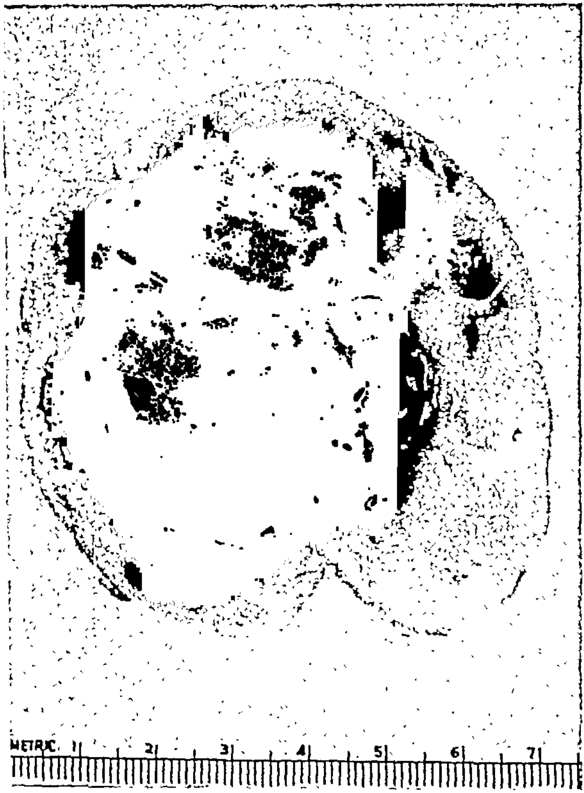


Fig. 6.

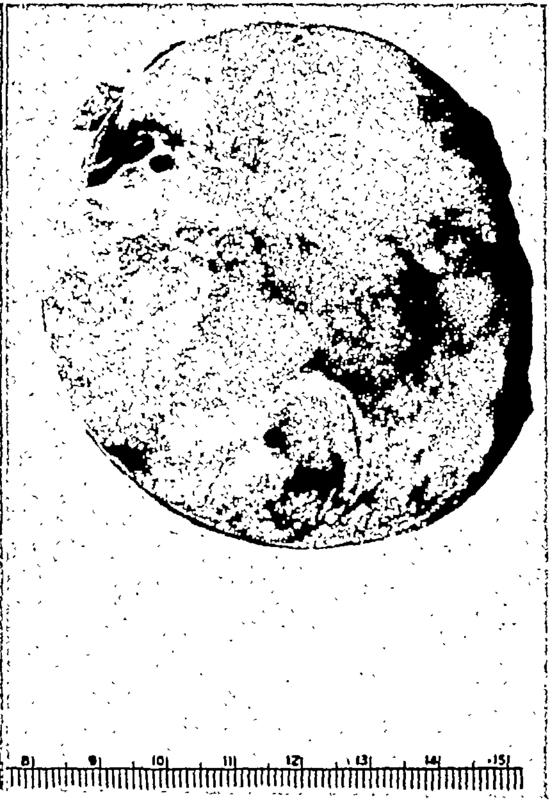


Fig. 7.

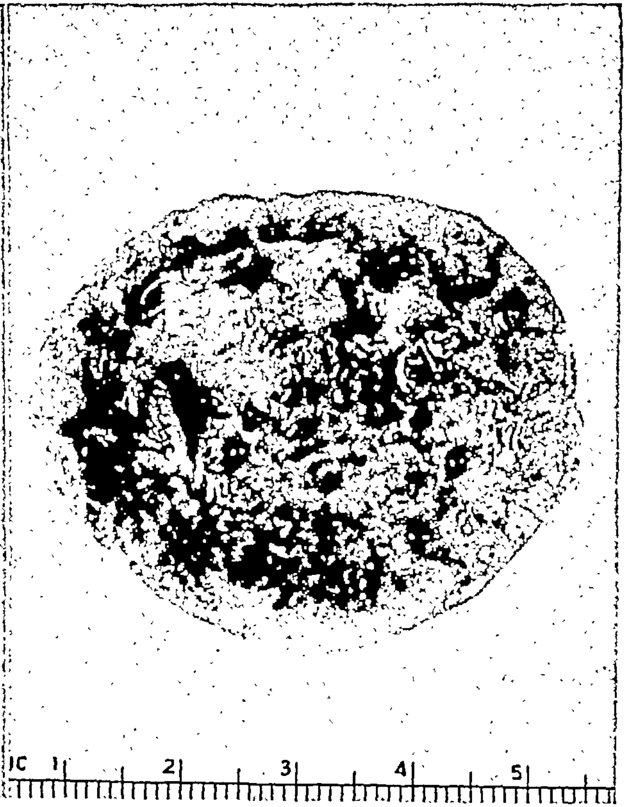


Fig. 8.

Fig. 6.—Encapsulated neurilemoma with areas of hemorrhage and necrosis.
Fig. 7.—Encapsulated neurilemoma. Light areas indicate zones of lipophages.
Fig. 8.—Encapsulated neurilemoma containing numerous vascular spaces simulating hemangioma.

tered within a nerve, making resection of the nerve compulsory for adequate removal. This lesion is usually not associated with von Recklinghausen's disease, although about 18 per cent[27] occur in frank or suspected cases of this disease. Ehrlich and Martin[20] found none of the stigmas of von Recklinghausen's disease in 12 cases of encapsulated neurilemoma of the head and neck. Material reviewed at Memorial Hospital by Vieta[25] indicated that the incidence of encapsulated neurilemoma in von Recklinghausen's disease is lower than 18 per cent. These tumors may reach huge proportions in the mediastinum and abdomen and undergo hemorrhage and cystic changes (Fig. 6). They may be yellow due to sudanophilic material (Fig. 7) or hemangiomatous because of numerous patulent vessels (Fig. 8). Microscopically, they are composed of Schwann cells, which may form Verocay nuclear rows (Antoni A) (Fig. 9), reticulated tissue (Antoni B) (Fig. 10), or a combination of the two. This last is the most frequent. A few neurites may be found near the former attachment to the nerve. Fibrous tissue varies in amount from area to area and tumor to tumor. Small round cells, plasma cells, and mast cells are seen in varying numbers. The blood supply may be so prominent that it suggests hemangioma (Fig. 11). The individual vessels show collagen collars, thrombosis, and subintimal lipophages. Extravasation of blood apparently occurs, since hemosiderin is occasionally present (Table II).

TABLE II. CERTAIN FEATURES OF ENCAPSULATED NEURILEMOMAS

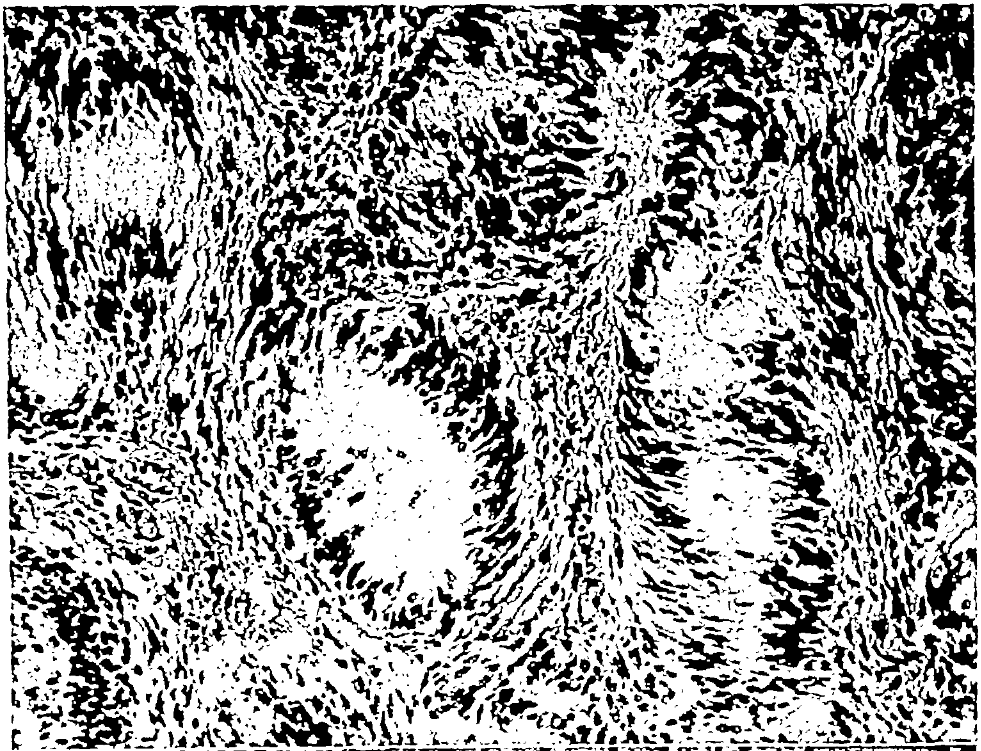
	LIPOPHAGES	PLEOMORPHISM	HEMOSIDERIN	VESSEL COLLARS
12 cases	8	8	4	10

Large numbers of lipophages (Fig. 12) may be found producing a pseudoxanthomatous appearance. The source of this fatty material is doubtful. It may be the result of hemorrhage or possibly be phagocytized myelin from degenerated myelinated fibers. Similar areas of lipophages are seen in these tumors in other locations.

Besides Antoni A and B and mixed encapsulated neurilemomas, the mediastinal tumors of this series included examples with an additional pattern. Several of the tumors were composed of closely packed, interlacing, and haphazardly arranged cells containing large hyperchromatic nuclei (Fig. 13). These features were so prominent that two of the lesions were classed as having equivocal changes of a type that might lead one to anticipate the possibilities of a recurrence and another was diagnosed as malignant neurilemoma (neurosarcoma). By virtue of adequate follow-up study these tumors are now known to be merely a pleomorphic variety of the encapsulated neurilemoma. It is this lesion that is most likely to be confused with malignant neurilemoma. Lesions from other locations may show a similar pleomorphic pattern and yield similar confusion.

Malignant neurilemoma (synonyms: neurogenic or neurogenous sarcoma, fibrosarcoma of nerve sheath, malignant neurinoma, malignant schwannoma) a tumor of Schwann cells, may arise apparently de novo or in diffuse neurilemoma (Fig. 14, *A* and *B*). It is generally considered not to occur in the encapsulated neurilemoma.[27, 20] In a large series of neurogenic sarcomas (malignant

Fig. 9.



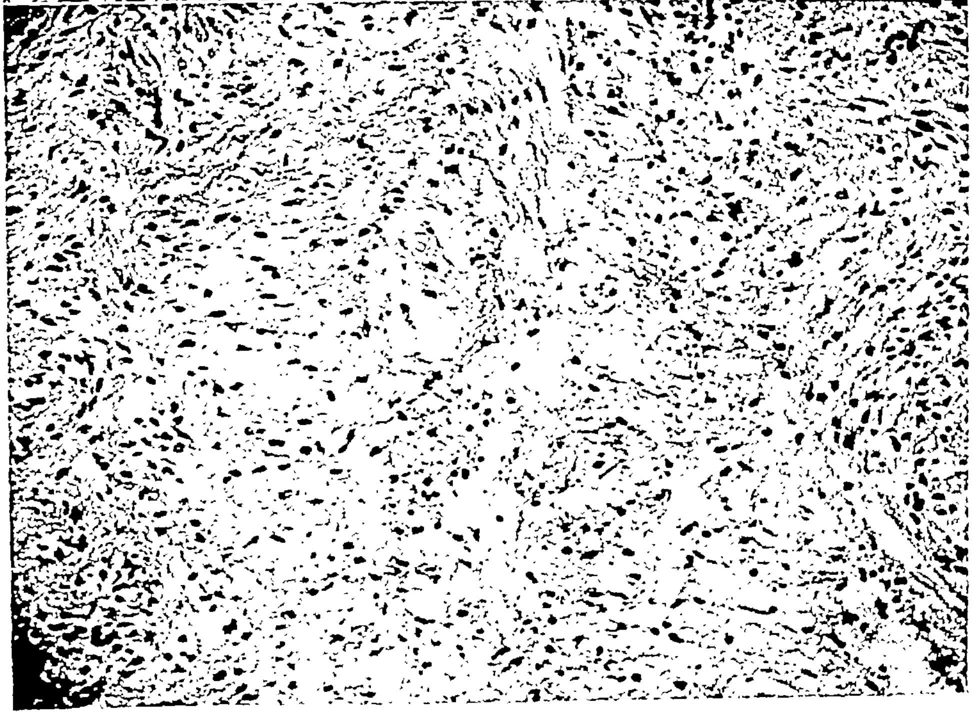
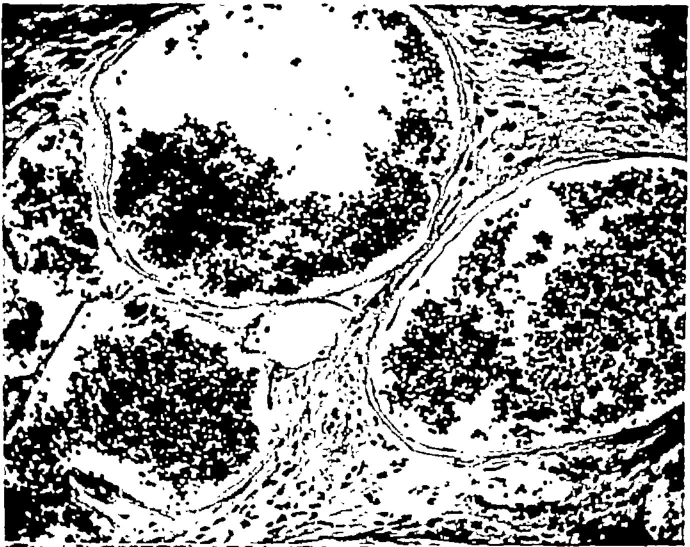


Fig. 10.

Fig. 9.—Encapsulated neurilemoma with palisading of nuclei (Antoni A).
Fig. 10.—Encapsulated neurilemoma with reticulated (Antoni B) areas.

Fig. 11.



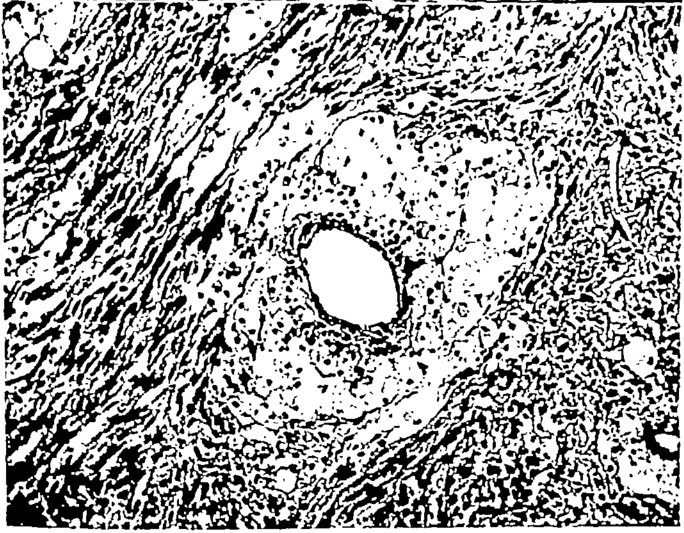


Fig. 12.

Fig. 11.—Encapsulated neurilemoma demonstrating thick vessel walls.
Fig. 12.—Encapsulated neurilemoma with perivascular lipophages.

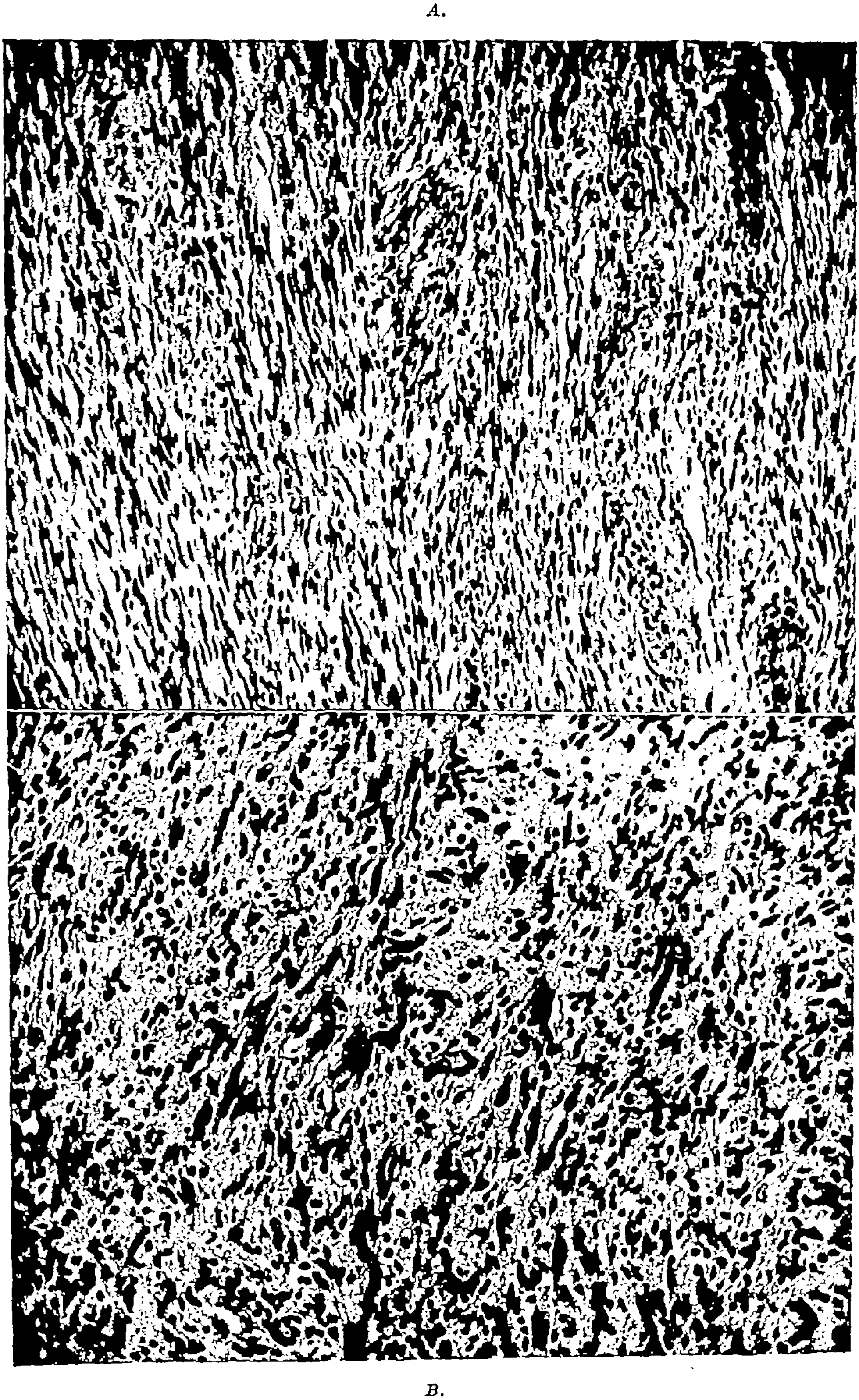


Fig. 13, *A* and *B*.—Encapsulated neurilemomas showing cellular pleomorphism.

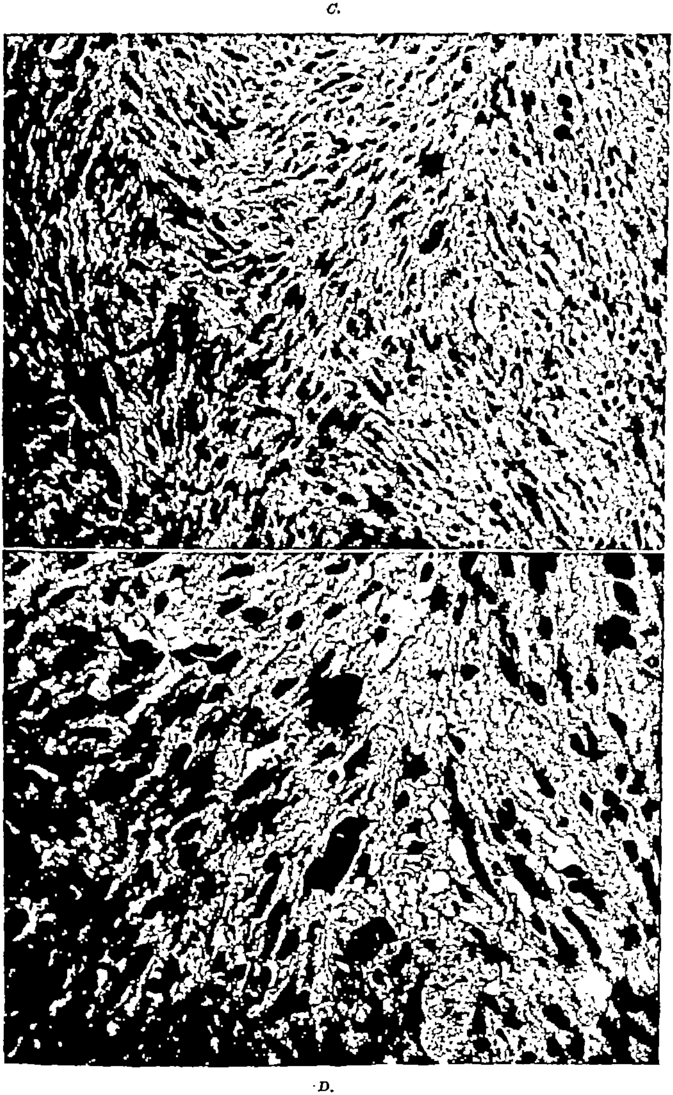


Fig. 11, *C* and *D*.—Encapsulated neurilemomas showing cellular pleomorphism.

ever, is nonspecific.[39, 40, 41] “While by definition it is possible for a paraganglion to arise from any part of the nervous system, our knowledge of concrete examples of paraganglia is confined to those which develop from the embryonic sympathetic nervous system—the adrenal medulla, the aortic bodies of Zuckerkandl and the chromaffin tissue found in the sympathetic ganglia.”[37] The term “paraganglia” may be used in a wider sense, including paraganglia that originate from other portions of the peripheral nervous system, such as

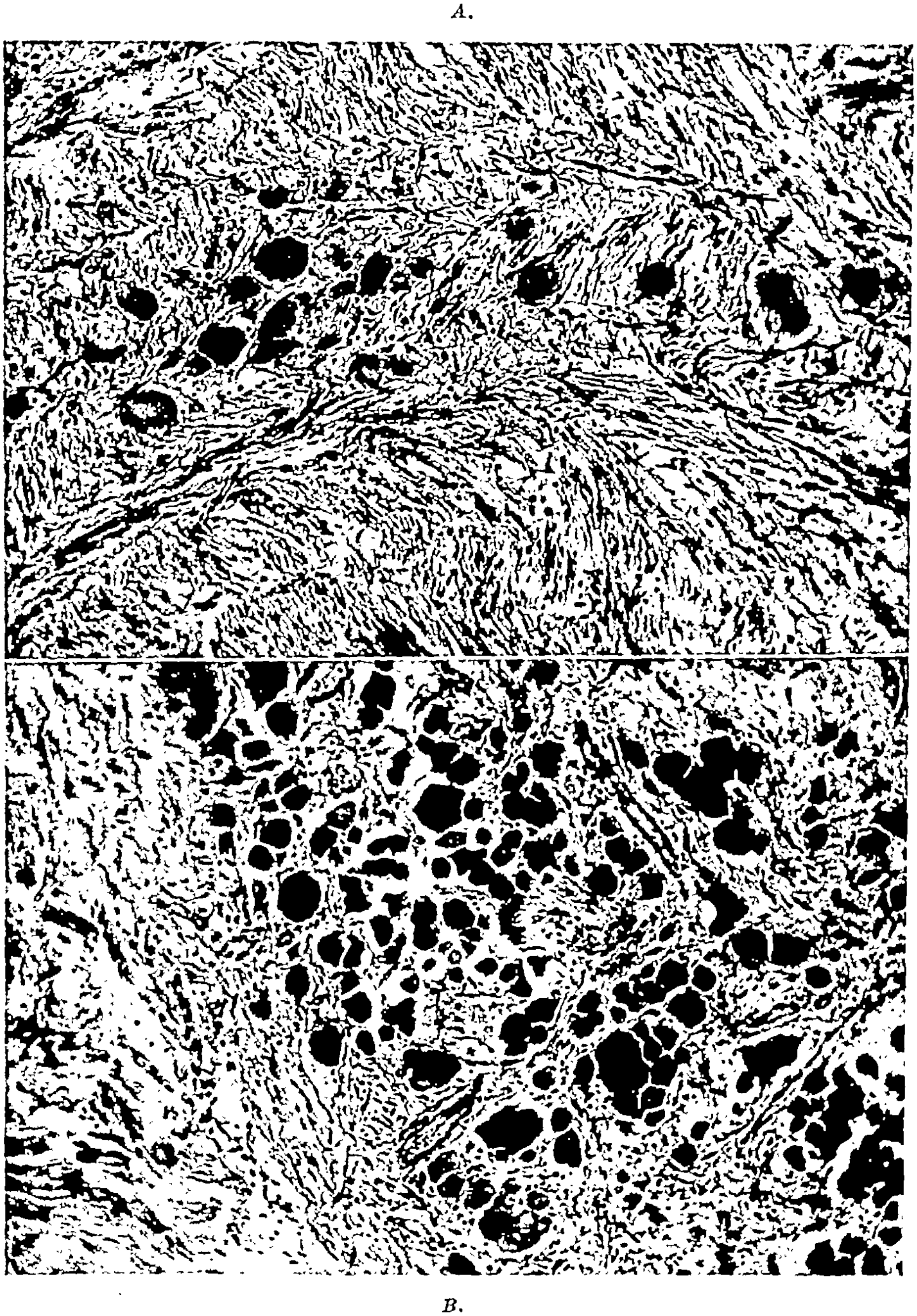


Fig. 18.—*A*, Ganglioneuroma showing general pattern. *B*, Ganglioneuroma showing variability of ganglion cells.

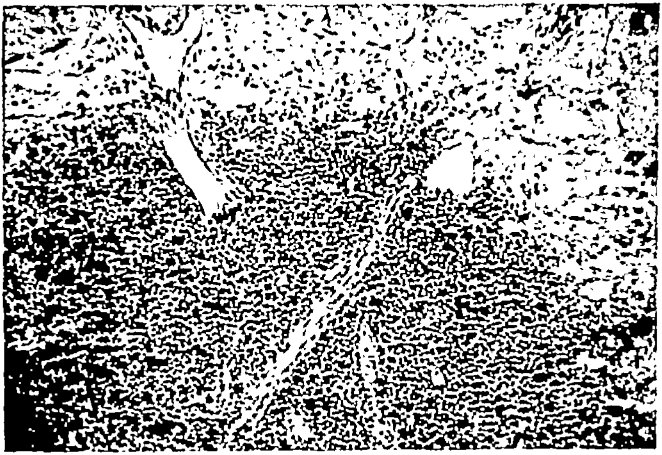


Fig. 19.—Focus of lymphoid cells found in neurilemoma and ganglioneuroma.

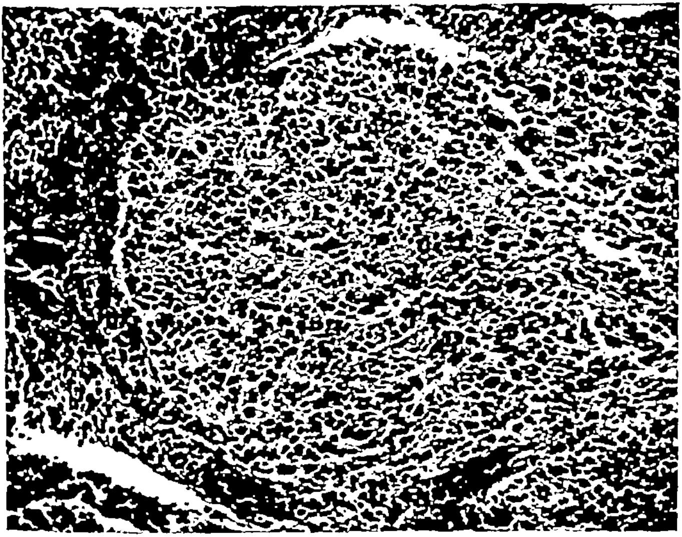


Fig. 20.—Sympathicoblastoma showing general pattern.

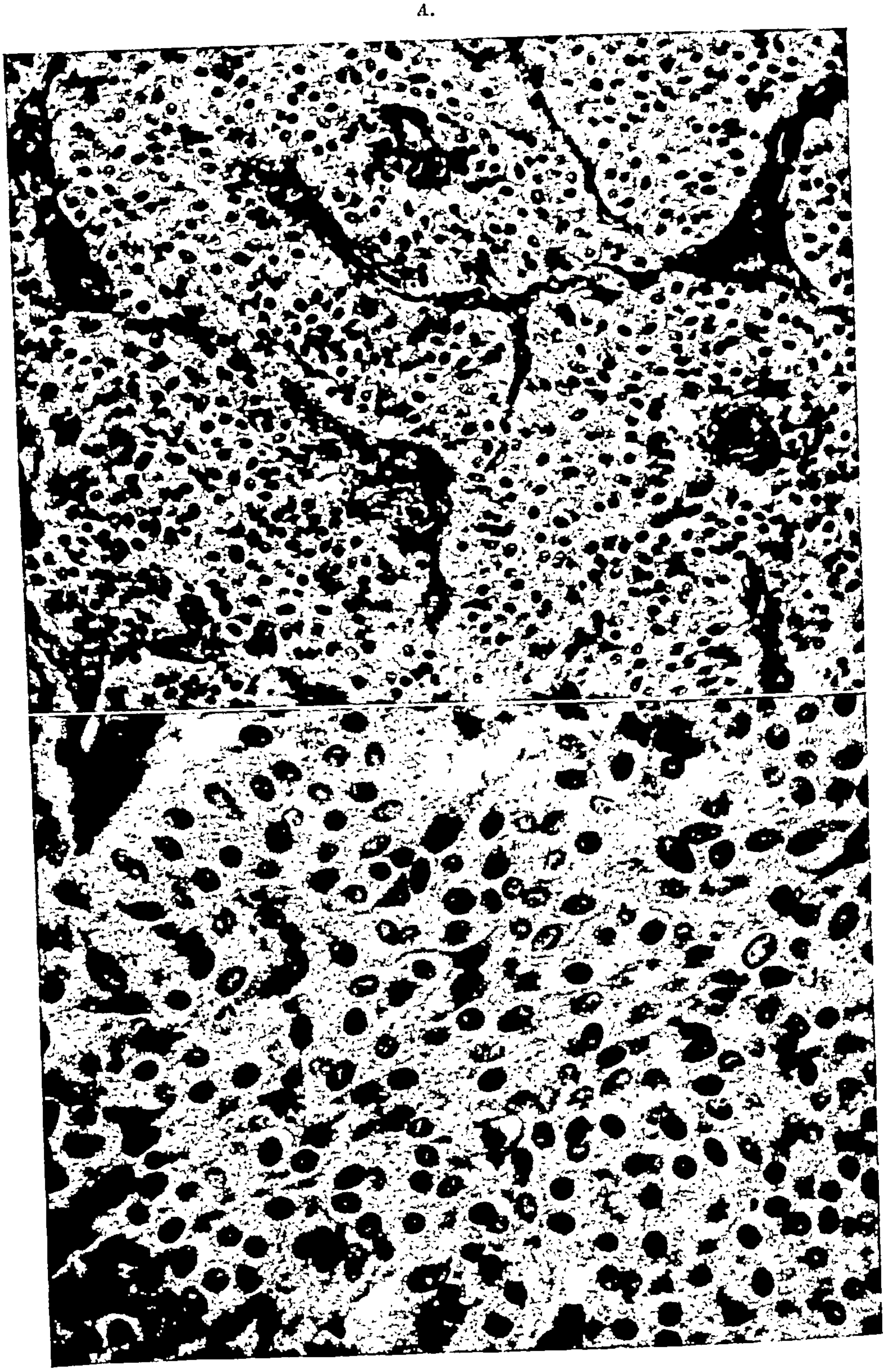


Fig. 21.—*A*, Paraganglioma showing general pattern. *B*, Paraganglioma showing uniform nuclei and indefinite cell walls.

the cranial nerves. We agree with Brines and Jennings[41] that the designation "paraganglioma" is preferable to pheochromocytoma or chromaffinoma owing to nonspecificity of the reduction of chromates, the absence of this reaction in many tumors, and the known histogenetic origin from paraganglion cells. These authors accept two tumors of previously reported intrathoracic paraganglioma. Recently, Maier[42] added another case. One other unreported case of the posterior mediastinum has been examined by one of us (J.T.G.).[43]

Grossly, the tumors may be large, encapsulated, reddish brown, soft, and show areas of necrosis.

The histologic picture varies from one resembling the adrenal medulla to one that is so atypical that diagnosis is a problem.

The cells may be arranged in cords or sheets and separated by a fine connective tissue (Fig. 21, *A* and *B*). The vascular component is usually abundant. The pheochrome reaction may or may not be positive and they may or may not be hormonally active. No malignant intrathoracic paragangliomas have been reported. However, McGavock and associates[44] accepted 8 cases of malignant paraganglioma from other anatomic locations. Cross and Pace[45] reported an additional case.

It should be mentioned that carotid-body tumors may be morphologically similar to paragangliomas; however, Boyd[37] is convinced that the carotid body and also the aortic-arch bodies should not be included as paraganglia.

Aortic-arch body tumors have been reported in dogs[46] and should be anticipated in man. Lattes[47] is reporting one aortic-arch body tumor in a paper on nonchromaffin paragangliomas to be published in *Cancer*. Several cases (dog) have been examined by one of us (J.T.G.) through the courtesy of Dr. R. Mulligan. Lattes and Waltner[48] have designated carotid-body tumors, glomus-jugulare tumors, and tumors of morphologically related tissues as nonchromaffin paragangliomas. This term could be applied to the tumor herein reported; however, as mentioned, the pheochrome reaction is nonspecific and not all true paragangliomas give the reaction. The identity of the morphologically related tissues as being true paraganglia is not established, in particular, the carotid and aortic-arch bodies as shown by Boyd.

Further work is essential for the clarification of histogenesis and function of these morphologically related tissues.

DISCUSSION AND CONCLUSIONS

The intrathoracic nerve-sheath tumors are predominantly encapsulated neurilemomas, of which there were 12 cases. They are benign, rarely, if ever, become malignant, and offer a good prognosis. One diffuse neurilemoma was encountered as the principal component of a teratoma. This patient died as the result of continued growth of the teratoma. One instance of malignant neurilemoma was found associated with von Recklinghausen's disease (diffuse neurilemoma) and this eventually resulted in the death of the patient.

Of the nerve-cell tumors there were 8 ganglioneuromas, all of which were differentiated. The prognosis of this lesion is good following removal. More adequate follow-up of this lesion is necessary in order to ascertain the prognosis in instances in which all of the tumor tissue has not been removed. A malignant course is not to be expected if the tumor is of the differentiated variety, which is the usual type found in the mediastinum.

There was one case of sympathicoblastoma thought to be primary in the mediastinum but not proved by autopsy. One paraganglioma was encountered that was hormonally inactive and pheochrome negative. This was a benign tumor and the prognosis is good. The possibility of this lesion being an aortic-arch body tumor was considered; however, it appeared too intimately related to the sympathetic chain to be other than a paraganglioma.

In this series of 24 neurogenic tumors 2 (8.33 per cent) were malignant.

SUMMARY

Twenty-four primary intrathoracic neurogenic tumors are reported with special emphasis on the pathologic features and classification. Two of the 24 cases were malignant. A new case of intrathoracic paraganglioma is included.

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DISCUSSION

DR. HERBERT C. MAIER, New York.—There are a few points that I should like to emphasize. We have had 3 cases of benign neurogenic tumor in the apex of the thorax that have extended into the neck and encircled the subclavian artery. In such cases the approach through the thorax may be relatively unsatisfactory, because one is unable to remove the cervical portion. Therefore, in the last of these 3 patients I employed an incision similar to a posterior thoracoplasty incision, except that I extended it further upward, and was able thus to remove that part of the tumor which extended into the posterior cervical region as well as the main mass through an extrapleural approach.

(Slide.) This is the x-ray of such a patient, and the next slide shows the groove that may be produced by the subclavian artery. Since these were benign tumors I split the capsule and along a septum and removed the tumor in that manner from around the subclavian artery.

(Slide.) This is a case of sympathicoblastoma that presented the unusual initial finding of a massive hemothorax. This film was taken after the hemothorax had cleared and, at that time, the etiology of the hemothorax was unknown as the tumor was not visualized on the roentgenogram. Some months later (slide) one could see a small round mass in the diaphragmatic region, and the lateral film shows the tumor to be somewhat further forward than most neurogenic tumors. As Dr. Pool mentioned, the sympathicoblastoma is a malignant tumor. This particular patient is well after two years.

DR. EARLE B. KAY, Cleveland.—I should like to discuss the technical aspects of operation of two types of neurofibroma; the cirsoid or plexiform neurofibroma and the dumbbell type of ganglionated neurofibroma that appears in children.

(Slide.) This demonstrates the extensive neurofibromatous infiltration in the apex of the left chest, with rib erosion, vertebral erosion, and the ribs separated. This was a 19-year-old boy. It was considered possibly malignant preoperatively, but it was known too that benign tumors could erode ribs as well.

(Slide.) The patient was explored through the fifth interspace. An extensive plexiform (cirsoid) neurofibroma was found infiltrating the brachial plexus, subclavian vessels, and the entire upper chest wall.

(Slide.) Some of these may be very extensive. It is a question how radical the operation should be. In this instance the entire upper five ribs were removed, leaving the subclavian vessels and brachial plexus along with the overlying muscles.

(Slide.) Next is the question of closure with such a large residual defect of the chest wall. The scapula bridged over the large defect. Only the muscles and soft tissues were closed. There has been no significant resulting defect.

(Slide.) This illustrates an example of the dumbbell neurofibromas seen in children. They are usually seen as a result of being asked by the orthopedist or neurosurgeon in consultation, because of spastic paraplegia. The question arises as to how they should be attacked. Should they have a laminectomy and the interdural aspect of the tumor removed first, or should they have a thoracotomy and the interpleural aspect removed?

(Slide.) In two cases laminectomy was performed first and the intradural aspect was removed; subsequently, after about two weeks, the intrapleural part was removed. At that time it is difficult to ascertain what is tumor and what is perhaps scar tissue. In the last two cases the thoracotomy has been the initial procedure, with removal of the intrapleural tumor. The spinal foramina can then be enlarged, or the intervening bone can be removed to allow removal of the intradural projection of the tumor. I think probably in most cases the tumor can be more effectively treated in this manner.

DR. DE WITT C. DAUGHTRY, Miami.—This is an interesting topic and I should like to show a couple of cases to illustrate that these lesions do not fall into a definite pattern, as you have already seen. Out of 13 cases, there were 2 with lesions extending through the foramina and compressing the spinal cord.

(Slide.) This roentgenogram shows multiple ganglioneuromas, two on the right and three on the left.

(Slide.) This is another roentgenogram of the same patient, showing three lesions on the left, two on the opposite side, and one below the diaphragm.

(Slide.) This is the roentgenogram of another patient, which shows in the apex of the right thorax a ganglioneuroma producing a considerable amount of pain for the size of the lesion. Upon exploration it proved to be a well-encapsulated, vascular lesion which seemed to pulsate when palpated. It was thought that this might be an aneurysm, and a needle was placed into it and 20 c.c. of bright red blood were aspirated. It was further freed and found to be not an aneurysm but a ganglioneuroma.

(Slide.) On cut section you can see the hemangiomatous type center, which gave the mistaken idea that it might possibly be an aneurysm.

In none of the 13 cases mentioned was malignancy found.

DR. POOL (closing).—I should like to thank the discussors, and to mention one point. In the group with ganglioneuromas, 8 patients were operated upon; 5 had partial excision. We felt that in these benign lesions partial excision was much safer where the lesion crossed the midline or was too extensive between the ribs. None of those tumors have shown further growth in the ensuing follow-up period—the longest period being four years. Whether partial excision is safe in a ganglioneuroma, only further time will tell.

TUMORS OF THE THYMUS

William D. Seybold, M.D.,* John R. McDonald, M.D.,†
O. Theron Clagett, M.D.,‡ and (by invitation) C. Allen Good, M.D.§
Rochester, Minn.

A NUMBER of factors lend fascination and serve to heighten interest in the study of tumors of the thymus. Perhaps of first importance in this regard are the mysteries of origin of the thymic elements, the mysteries of the function of the gland, and the mysteries of the general alterations of the gland in disease. Likewise, interest comes from the obscure and tantalizing association of tumors of the thymus with myasthenia gravis, an association well known to us all, but understood by no one. It is hard to dismiss the occurrence of thymic tumors in 15 per cent of patients with myasthenia gravis[1] as simple coincidence. Nevertheless, little progress has been made in our understanding of this association during the past forty-nine years since Weigert[2] first reported a case of myasthenia gravis associated with a thymic tumor. Finally, of absorbing interest are unique clinical and pathologic features of the thymomas, a group of tumors about which much confusion and controversy center.

The controversies concerning classification and the variety of classifications that have been proposed for neoplasms of the thymus are the natural sequel of the incomplete knowledge of the origin of the cellular elements of the normal thymic parenchyma, and the common mistake of assigning a thymic origin to all tumors which are located in the anterior mediastinum. Since the small round cells of the thymus are morphologically identical with lymphocytes, the differentiation of tumors of the thymus arising from or composed almost completely of these cells, from tumors arising from lymph nodes in the anterior mediastinum may be difficult. The presence of these cells in large numbers in many thymomas has led to the erroneous idea that these tumors are lymphoblastomas. Conversely, because these small cells are known to exist in the normal thymus and in tumors of the thymus, lymphoblastomas arising in the anterior mediastinum have been erroneously classified as thymic tumors. Some of the confusion in classification has been the result of the unwillingness of some writers to classify the small thymocytes as lymphocytes because they believe that the thymocytes have an epithelial origin,[3] although most workers believe that they are lymphocytes[4] which have wandered into the gland.[5]

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PLAN OF THE PRESENT STUDY

For this study, the records of those patients who registered at the Mayo Clinic during the period 1935 through 1949 and who had intrathoracic tumors of possible or probable thymic origin were reviewed. Only those cases in which tissue had been made available by surgical operation or by post-mortem examination were accepted for study; in this group, 45 patients had tumors which we classified as thymomas.

These cases of thymoma fell readily into two major groups clinically: those associated with myasthenia gravis and those unassociated with myasthenia gravis. Since, in our experience, 15 per cent of patients who have myasthenia gravis have a thymoma and 75.6 per cent of the patients with thymoma have myasthenia gravis, the division of our material on this basis for comparative analysis seemed sensible and challenging.

ANALYSIS OF CLINICAL DATA

In this small number of patients no essential difference in age could be made out in the two groups (Table I). By reason of the fact that approximately one-half of the patients with myasthenia gravis who come to the clinic are less than 40 years of age,[14] the occurrence of 22 (65 per cent) of the thymomas in association with myasthenia gravis in patients older than 40 years is probably significant.

TABLE I. CLINICAL FEATURES OF THYMOMA

CLINICAL DATA	PATIENTS WITH THYMOMA: MYASTHENIA GRAVIS	
	PRESENT (34)	ABSENT (11)
Age in years		
Extremes	26 to 68	16 to 65
Average	45.5	43.1
Sex		
Female	20	8
Male	14	3
Symptoms due to tumor		
Pain	4	4
Obstruction of superior vena cava	2	1*
Roentgenologic evidence of mediastinal tumor	33	11†

*This patient also experienced thoracic pain.
†Tumors of 7 of these patients were discovered by accident.

There was no significant difference in the sex incidence of thymomas in our series. In both groups of patients symptoms due to the presence of the tumor as such were exceptional. Since, with the exception of 1 tumor in this series, a thymoma is an anterior mediastinal lesion initially, it is not surprising that obstruction of the trachea or bronchi did not occur in any patient, or that signs of obstruction of the superior vena cava developed in three.

Of 34 patients with thymomas associated with myasthenia gravis, mediastinal tumors were demonstrated by roentgenologic means in thirty-three. In 1 patient the tumor was discovered only at the operation designed to remove the thymic gland in the hope that the course of the patient's myasthenia would be influenced favorably.

Pain in the chest was the result of involvement of the parietal layer of the pleura by the tumor. In view of the fact that complete surgical removal of the tumor was possible in only 3 of 8 patients who experienced pain in the thorax, the appearance of this symptom must be viewed with grave concern.

A possible relationship between hyperthyroidism and myasthenia gravis has been discussed by several writers.[26-28] With the exception of 1 patient with myasthenia who had a toxic adenomatous goiter, no endocrine disturbances were noted in any of our patients with thymomas.

ROENTGENOLOGIC DIAGNOSIS

There is nothing in the roentgenologic appearance of a thymoma to distinguish it from other tumors occurring in the anterior mediastinum. In all but 1 instance in our experience tumors of the thymus have been situated in the anterior portion of the mediastinum (Figs. 1 and 2). The 1 exception was a tumor found to lie posterior to the superior vena cava about midway between the sternum and the bodies of the thoracic vertebrae (Fig. 3). While the majority are situated anterior to the arch of the aorta and base of the heart this position is not constant; in our experience thymomas may be found at a level as low as the ninth or tenth thoracic vertebra, approaching the level of the diaphragm (Fig. 4).

The tumor is usually round or oval and sharply delineated from the surrounding tissue. In some instances, however, the mass may be somewhat flat and lie in close proximity to the anterior surface of the pericardium. In such cases the tumor appears as a bulge projecting forward from the cardiac shadow into the anterior mediastinum.

Sufficient calcium to be apparent roentgenologically was present in 13 of the 45 thymic tumors in our series (Fig. 4). It usually occupied a peripheral position, as though it were deposited in the wall of a cyst, but rarely it was distributed unevenly through the tumor, and in 1 case it seemed to be deposited in the central portion of the tumor. The presence of calcium in such quantities does not mean that the lesion is an innocent one, for in 1 case in which the tumor showed roentgenologic evidence of calcification, implants of tumor tissue were found on the pleural surface of the lung and diaphragm and on the posterior surface of the sternum. In another similar case the tumor had surrounded and obstructed the superior vena cava and had invaded the mediastinal pleura.

In 1947, one of us (Good[29]) reported on the roentgenologic recognition of thymic tumors in patients with myasthenia gravis. At that time it was noted that the ordinary posteroanterior roentgenogram of the thorax often failed to reveal a thymoma which subsequently could be found by roentgenoscopy or a roentgenogram made in the lateral projection (Fig. 1). Because of this fact all patients with myasthenia gravis seen at our institution are examined by means of roentgenoscopy and lateral roentgenograms, as well as the more routine posteroanterior stereoscopic pair. In a series of 249 consecutive patients with myasthenia gravis so examined, 37 tumors were found, an incidence of about 15 per cent.[30] Approximately 40 per cent of these tumors were not apparent on the roentgenogram made in the frontal projection. It is our opinion that all patients known to have, or suspected of having, myasthenia gravis should receive the benefit of the more detailed roentgenologic examination outlined previously, because of the observed incidence of thymic tumors in this disease.

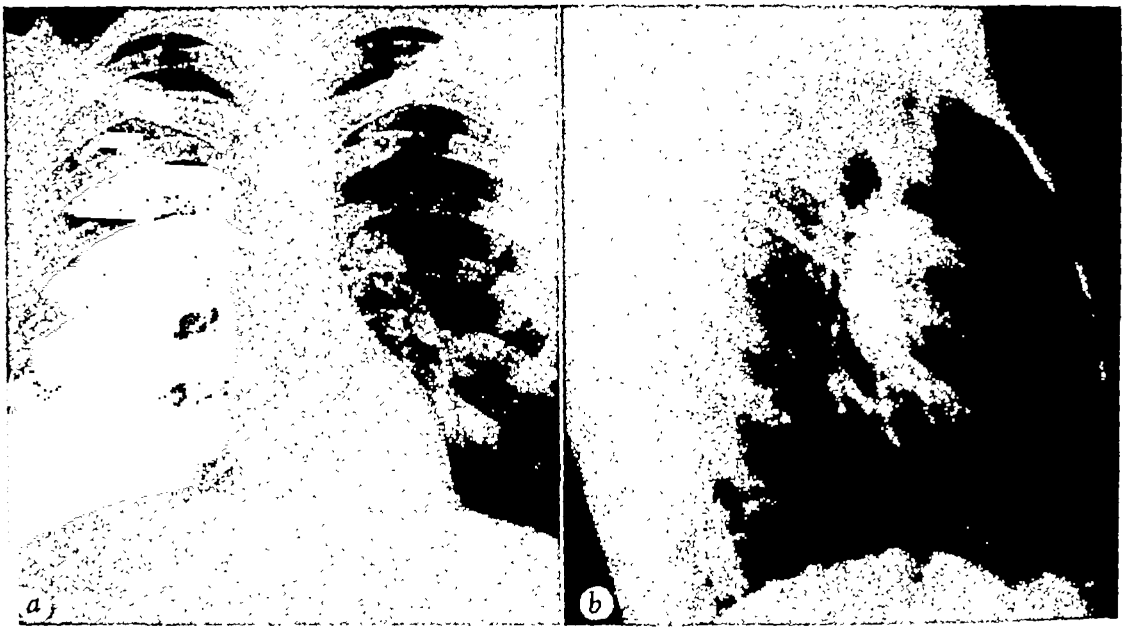

Fig. 1.—*a*, Posteroanterior view shows normal mediastinal shadow. *b*, Lateral view demonstrates a definite shadow in the anterior mediastinum at the level of the aortic arch.

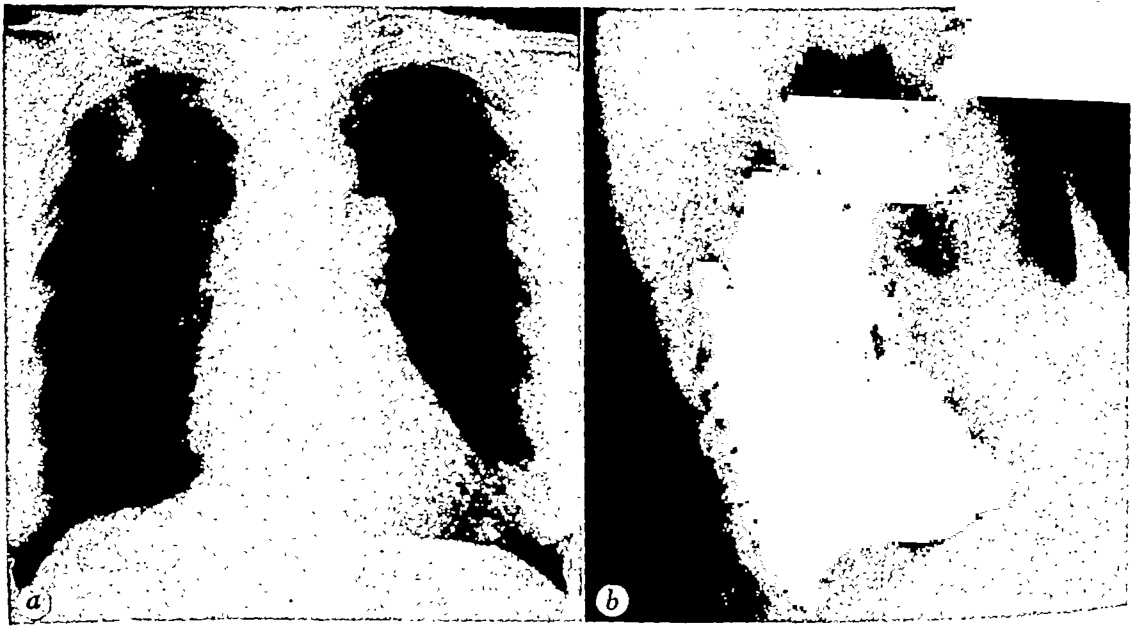

Fig. 2, *a* and *b*.—Anterior superior mediastinal tumor which proved to be a thymoma.

Although the roentgenologic appearance of a thymic tumor is not sufficiently characteristic to allow it to be distinguished from other tumors of the anterior mediastinum, the presence of a tumor in this location in a patient with myasthenia gravis makes a diagnosis of thymoma almost certain. We have never encountered a tumor in the anterior mediastinum of a patient with myasthenia gravis which proved to be anything other than a thymoma.

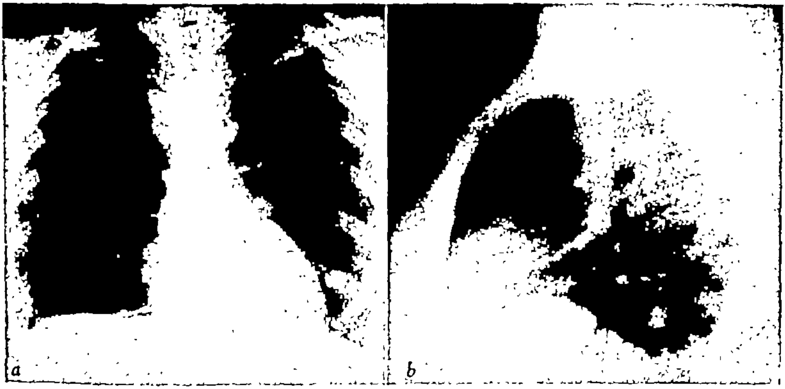

Fig. 3, *a* and *b*.—The shadow of a tumor which proved to be a thymoma can be seen in the middle and posterior portion of the superior mediastinum.

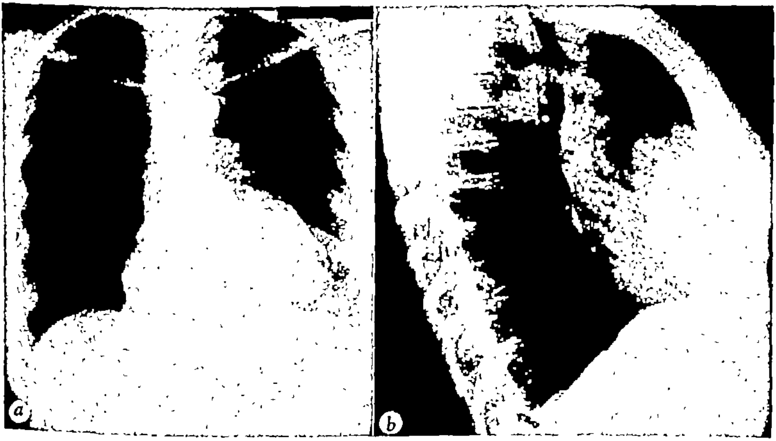

Fig. 4, *a* and *b*.—Anterior inferior mediastinal tumor which proved to be an encapsulated thymoma. Calcium is present.

PATHOLOGIC CHARACTERISTICS

We believe that much of the past and present confusion in the classification of tumors of the thymus has been due to the inclusion, by a number of authors, of tumors that were not primary in the thymus but which arose primarily in the lung as bronchiogenic carcinoma, which were mediastinal manifestations of a generalized disease of the lymphatic system, or which were mediastinal teratomas. The perusal of case reports in the older literature leaves little doubt in the mind of the modern reader who is familiar with the pathology of bronchiogenic carcinoma that many of the latter of the small-cell or oat-cell type have been classified as malignant thymic tumors. Specifically we would mention the cases reported by Symmers[18] in 1932, most of which we would interpret differently today. Study of his case abstracts reveals that of the 8 patients whose tumors were called "peritheliomas," 6 were middle-aged men whose illness at the onset was characterized by respiratory symptoms: cough, "grippe," hemoptysis, and dyspnea. Extensive involvement of a lung and major or minor bronchi was described in 6 patients. It seems probable to us that these patients were victims of bronchiogenic carcinomas of the small-cell variety rather than of malignant tumors that arose in the thymus.

Our concept of the primary thymic tumors limits the group to those mediastinal tumors which are characterized histologically by the presence of both thymic epithelial (reticulum) cells and thymocytes in varying proportion. Such a concept not only fits our own material, but it provides a basis for understanding why some of the true thymomas have been described as lymphosarcomas and others as epitheliomas. The designation for the tumors in which the small round cell predominates almost to the exclusion of the epithelial cell has commonly been that of lymphosarcoma,[3] while for those tumors in which the reverse proportion exists, the diagnosis has usually been carcinoma or epithelioma.

On the basis of gross or microscopic examination the thymoma which has been removed from the patient with myasthenia gravis cannot be distinguished from the one which has been removed from the patient who is unaffected by this malady; but, while there is uniformity within wide but well-defined limits in the histologic pattern of all these thymomas, there is a great variation in the gross character of the tumors, some being solid, some being partially or almost completely cystic, the majority being encapsulated, but some being invasive and capable of surface implantation.

Deposits of calcium are fairly common in thymomas, both in the encapsulated and in the invasive and implanting varieties.

Gross Appearance.—(Fig. 5.) Grossly, a typical thymoma is a lobulated tumor with a thick, fibrous capsule which is complete (Fig. 5, *a*), but in almost a fourth of the tumors in our study the capsule was incomplete, and the tumor had invaded contiguous structures in the mediastinum. The most striking feature of the grayish-pink, cut surface of the average thymoma was lobulation produced by fibrous trabeculae (Fig. 5, *c*). Not all tumors, however, were lobulated (Fig. 5, *b*).

Cystic changes were present in most of the tumors (Fig. 5, *d*). The size and the number of cysts varied greatly, and in 3 instances no viable tumor cells could be identified in the walls of completely cystic thymic tumors removed from patients with myasthenia gravis. This complete absence of neoplastic tissue made absolute determination of the nature of the tumors impossible, but we feel that by inference they can be and should be grouped with thymomas. The preparation and study of many sections from 1 tumor that appeared to

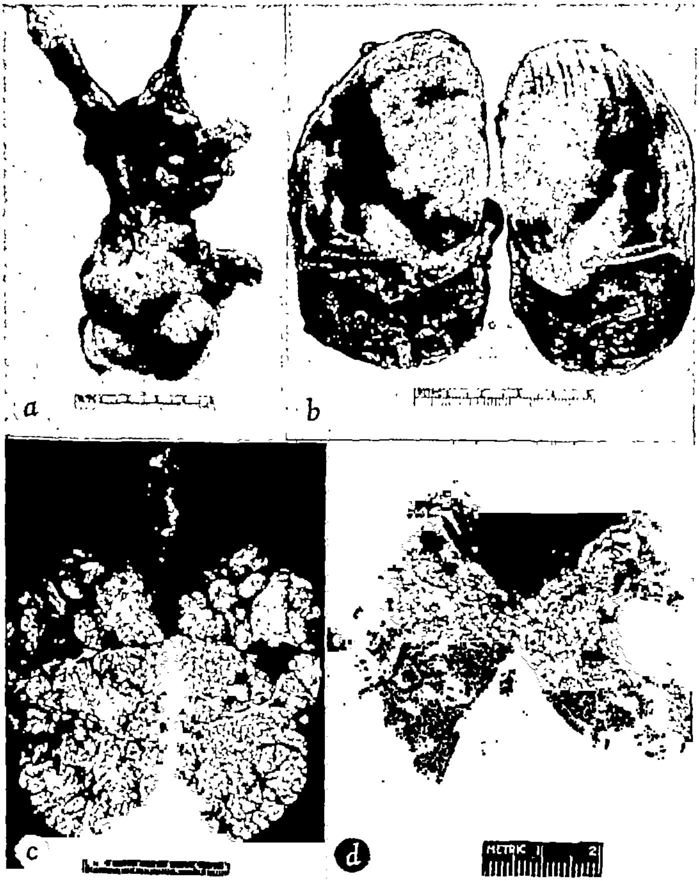

FIG. 5.—*a*, Thymus and thymoma from a patient with myasthenia gravis. *b*, Thymoma unassociated with myasthenia gravis. The capsule and a hemorrhagic cyst can be seen. *c*, Thymoma unassociated with myasthenia gravis. Lobulation and fibrous trabeculation are evident. *d*, Thymoma showing extensive cystic change. The patient had myasthenia gravis.

be completely cystic permitted a histologic diagnosis of thymoma. These cysts often contained a thick whitish material having the consistency of putty; less often they contained blood. Particularly in the tumors which were cystic, calcium deposits in the capsule and trabeculae were common.

Histopathologic Aspects.—The constant histologic feature of this group of 42 thymomas, excluding the 3 in which no viable neoplasm could be found, was the presence of the two cell types of the normal thymic parenchyma: the thymocyte and the epithelial cell (Fig. 6). The thymocyte is morphologically identical with the mature lymphocyte. The epithelial cell has often been called a reticulum cell in the thymus because of its similarity to reticulum cells in other organs. These epithelial cells usually have a distinct, pale nucleus with small nucleoli, varying amounts of cytoplasm, and indistinct cell membranes. In some of the tumors of our series epithelial cells had nuclei which were small and dark stained; in others these cells had foamy cytoplasm. Although the presence of both thymocytic and epithelial cells was invariable, the relative proportion of these cells varied widely from tumor to tumor and from place to place in the same tumor.

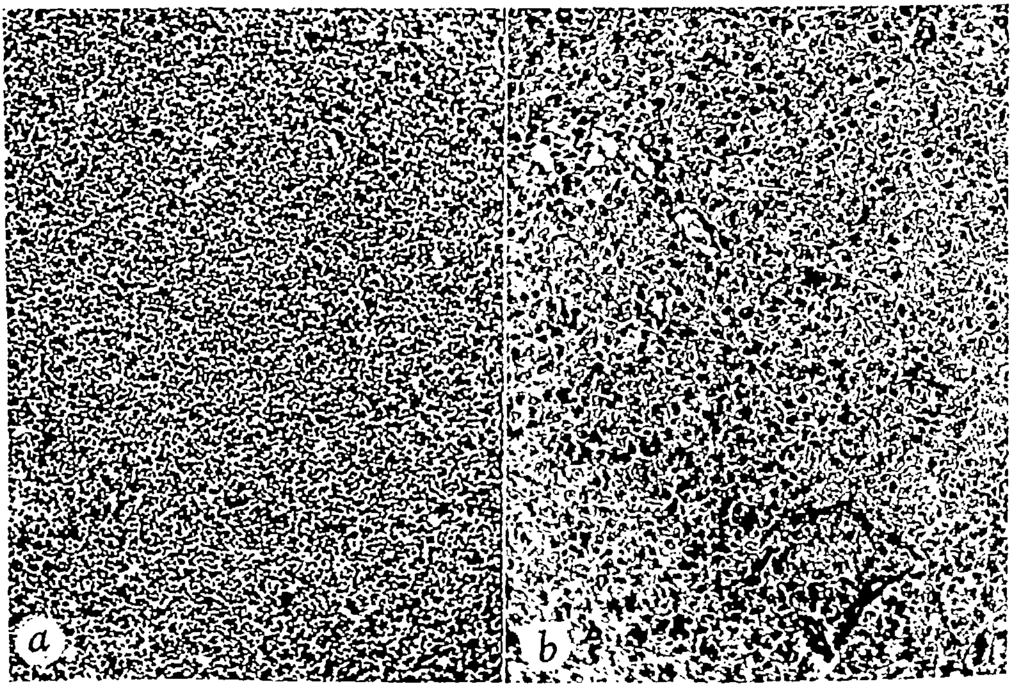

Fig. 6.—Thymoma (hematoxylin and eosin ×100). *a*, The thymocyte is the dominant cell in this tumor. *b*, The epithelial cell is the dominant cell.

Next in the order of importance as a distinctive histologic feature of thymomas was a palisaded arrangement of the epithelial cells about spaces, vessels, and fibrous trabeculae. This feature was present in 25 cases. A secretory function for the epithelial cells lining the cystic spaces was suggested to us by the presence of an acellular fluid in many of the spaces. This concept is consistent with the generally accepted idea that these cells are of an epithelial nature. In parts of the tumor containing many of these adenomatoid structures, lumina of many sizes could be seen; some of these did not contain fluid (Fig. 7, *a* and *b*), while others did (Fig. 7, *c*). Hemorrhagic material in some cysts was undergoing organization (Fig. 7, *d*).

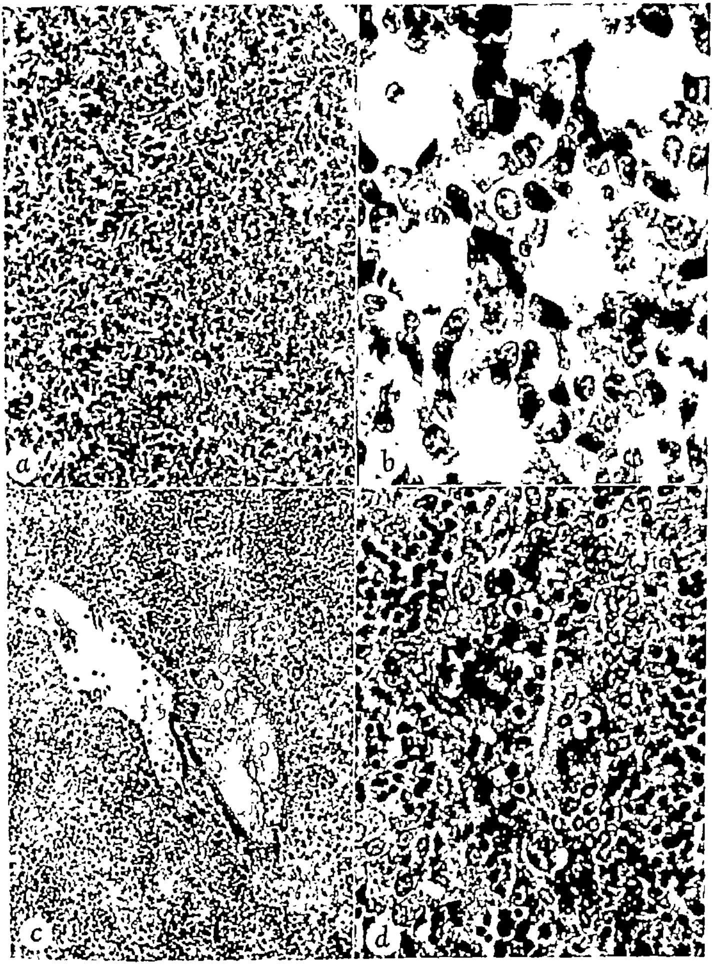

Fig. 7.—Thymoma (stained with hematoxylin and eosin). *a* and *b*, The adenomatoid arrangement of the epithelial cells is apparent. (*a*, ×165; *b*, ×880.) *c*, The epithelial cells have formed two "acini." The fluid in the one on the right is hemorrhagic (×100). *d*, The hemorrhagic fluid in the lumen of an "acinus" is organizing and in the left part of the acinus a small capillary is evident (×365).

The occurrence of these epithelial cells in palisade arrangement about spaces, about blood vessels imbedded in loose areolar tissue (Fig. 8, *a*), and about fibrous trabeculae (Fig. 8, *b*) suggested to us the possibility that these three features represent successive stages in a single process which begins with organization within the space. Perhaps hemorrhage which is rather frequent in these spaces provides the soil for the process of organization. Although palisading

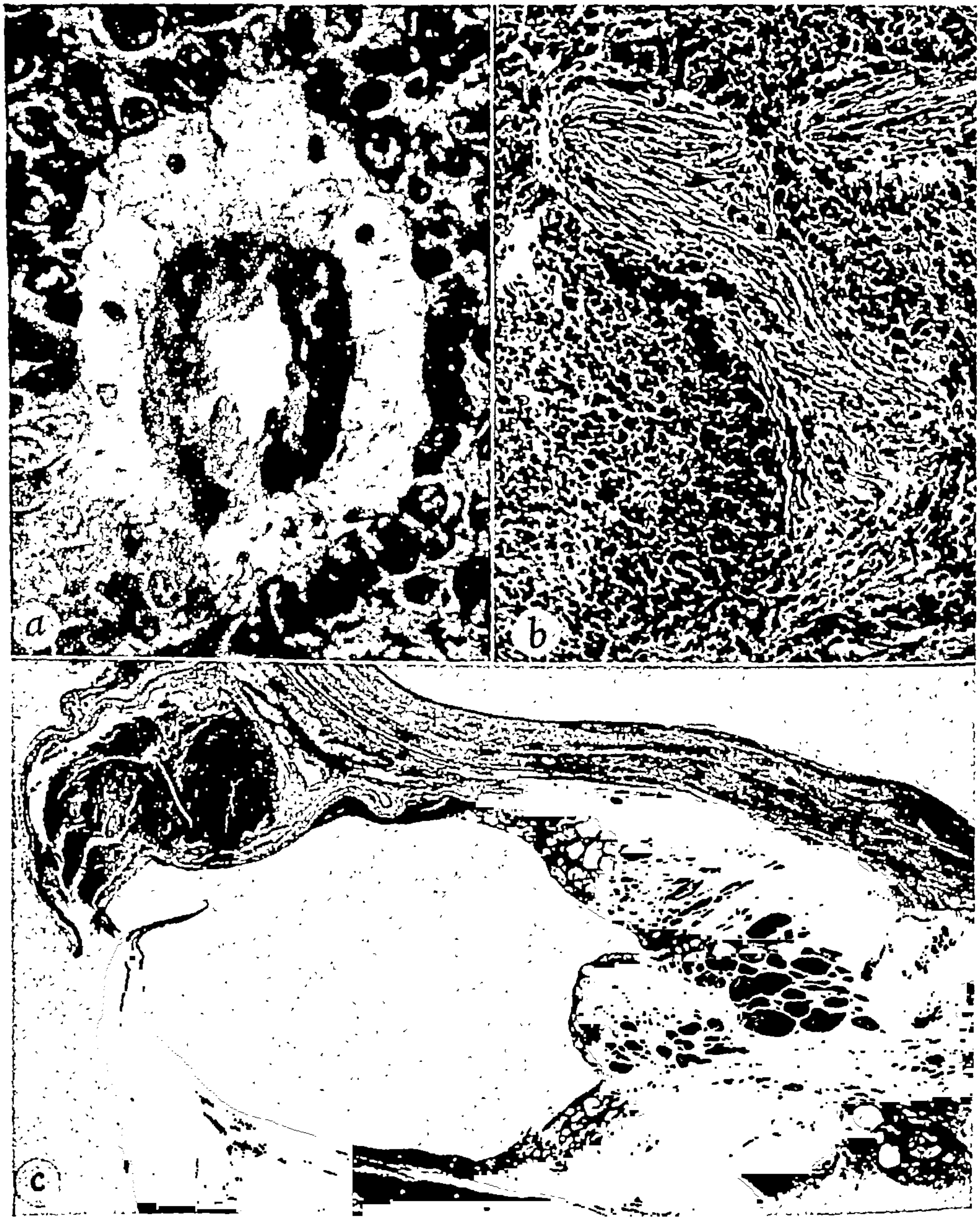

Fig. 8.—Thymoma. Stained with hematoxylin and eosin. *a*, Vessel surrounded by areolar tissue with palisaded epithelial cells (×500). *b*, Fibrous trabecula with the epithelial cells palisaded at right angles to the long axis of the trabecula (×165). *c*, Typical thick fibrous capsule and cystic spaces, some of them small, some quite large, lined by epithelial cells (×5).

was a frequent phenomenon about fibrous trabeculae it was not constant in our series.

Gross cystic changes (Fig. 8, *c*) in thymomas can be accounted in two ways: (1) on the basis of the progressive accumulation of fluid in these adenomatoid spaces either as a result of secretion or hemorrhage and (2) as a result of infarction with resulting liquefaction necrosis.

Hassall's corpuscles, the most characteristic feature of the adult human thymus, were present in only 11 of the thymomas in our series. A number of the structures which we called immature Hassall's corpuscles were whorls of epithelial cells (Fig. 9, *a*), but more often they were typical in appearance and a number were calcified (Fig. 9, *b*).

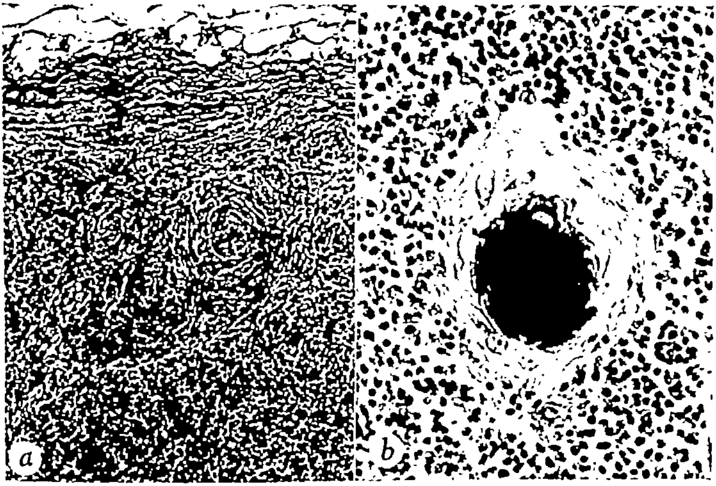

Fig. 9.—Thymoma. Stained with hematoxylin and eosin. *a*, Immature Hassall's corpuscles (×150). *b*, Mature Hassall's corpuscles with calcification (×365).

In 1 encapsulated thymoma the cell pattern was characteristic except for the presence of cells with multilobulated nuclei and pink-staining nucleoli that resembled Reed-Sternberg cells of Hodgkin's disease (Fig. 10, *a*). It seems likely that these were only variants of the epithelial cells.

The structure of the secondary deposits from the 2 tumors which spread by implantation to pleural surfaces was almost identical with that of the primary tumor; fibrous trabeculae were present and the same proportion of the two essential cells was preserved (Fig. 10, *b* and *c*).

Generally speaking, histologic features of malignancy were absent. In all tumors the epithelial cells had sharp perinuclear membranes; they were regular in size and showed little hyperchromasia. Rare mitotic figures were seen in only a few tumors. Foam cells and cholesterol crystals were present, particularly in necrotic and degenerated sites. The thymocytic cells in all tumors resembled adult lymphocytes.

Tumor Behavior.—In several respects the behavior of these tumors is unusual. While most tumors which extend by invasion, also metastasize by the blood or lymph stream, thymomas seem to be an exception. Although in our series 10 of 45 tumors invaded contiguous structures and 2 spread to pleural

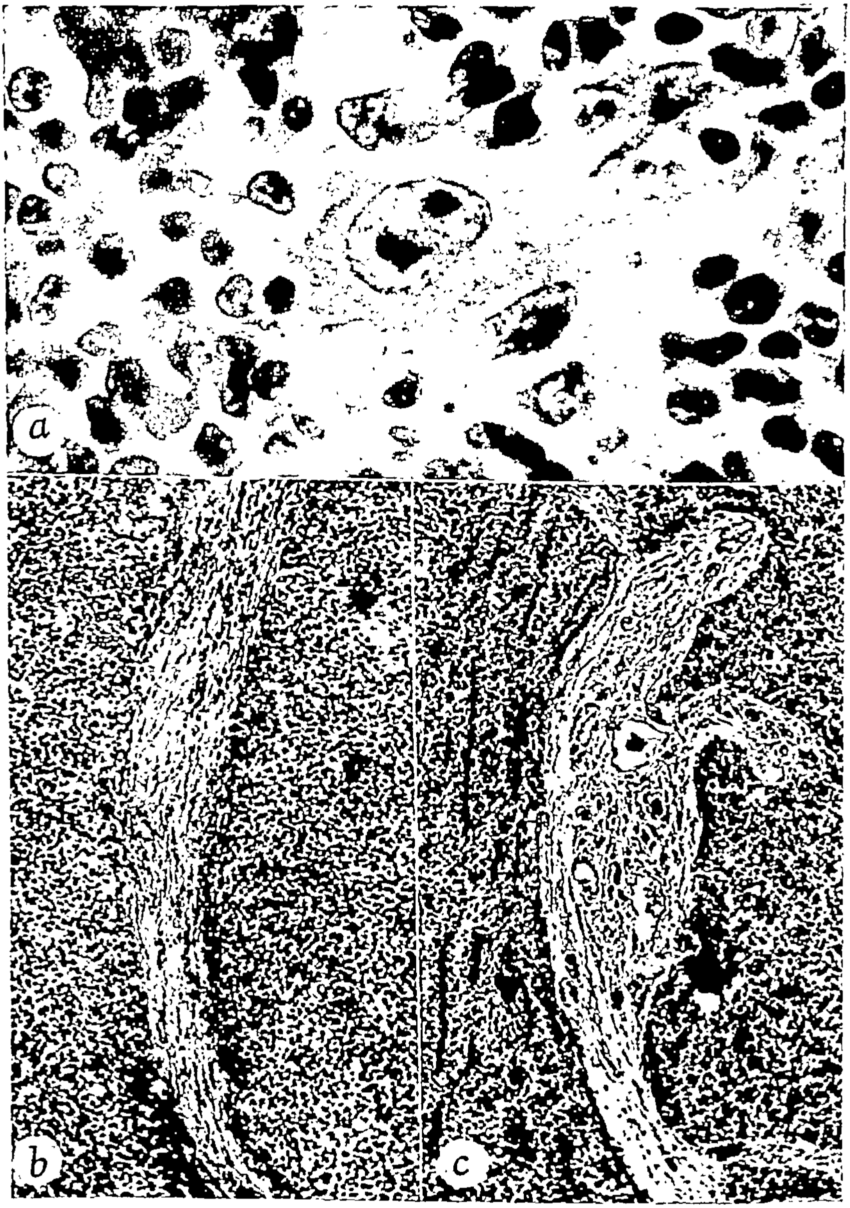

Fig. 10.—Thymoma. Stained with hematoxylin and eosin. *a*, Cell with a multilobulated nucleus that resembles a Reed-Sternberg cell (×1,040). Such cells were present in only one tumor. *b*, Primary tumor demonstrating fibrous trabeculae and the mixture of thymocytic and epithelial cells (×100). *c*, Pleural implant showing a histologic pattern similar to that of the primary tumor (×100).

TABLE II. MODE OF EXTENSION OF THYMOMA IN 11 CASES

	CASES
Invasion of	
Pleura	0
Pericardium	5
Superior vena cava and innominate veins	5
Lung	3*
Implantation to parietal and visceral pleura	2

*Only the superficial aspects of the lobe adjacent to the mediastinal tumor were involved.

surfaces by implantation, none produced embolic metastasis (Table II). The histologic appearance of these tumors which had extended to other structures differed in no particular from that of the tumors which were completely encapsulated. Furthermore, the tumors of the patients who had myasthenia gravis seemed to behave exactly like those which were unassociated with myasthenia.

The tendency of these tumors to extend by invasion and by implantation has been described by previous authors.[10, 12-16] Obstruction of the superior vena cava and the innominate veins is the result of compression by the tumor in some patients, but actual invasion of the venous wall does occur. We have been unable, however, to find evidence of extension of the tumor into the lumen of the vein. Since most of these tumors lie in contact with the pericardium, it is not surprising to find that it is involved frequently by the invasive tumors. One tumor had extended through the fibrous pericardium to form a mass within the pericardial sac.

Complete necropsies were done in 11 cases. In none was there evidence of lymphogenous or hematogenous metastasis. It is worth mentioning that lymphorrhages which are common in the skeletal muscle of patients with myasthenia gravis may be mistaken for metastatic lesions. Such a mistake accounts for some of the reports of embolic metastasis that are to be found in the literature.

Rate of Growth—There is much evidence that thymomas are slow-growing tumors, both in the patients who have myasthenia gravis and in those who do not. In our series, of the patients in the former group 1 was known to have a mediastinal tumor ten years, and another five and one-half years prior to

TABLE III. FATE OF PATIENTS WITH INERADICABLE THYMOMA

	PATIENTS WITH THYMOMA: MYASTHENIA GRAVIS	
PRESENT STATUS	PRESENT	ABSENT
Dead	5	0
Died while in hospital	2	0
Died since dismissal	3	0
Alive	1	3
Condition satisfactory	1*	1†
Condition worse	0	2‡
Lost to follow-up	0	1§
Total	6	4

*Fifty months after operation.

†Six months after operation.

‡Each patient survived nineteen months after operation.

§This patient had an ineradicable lesion in 1946 and, letters of inquiry remaining unanswered, is presumably dead.

TABLE IV. SURGICAL TREATMENT OF THYMOMA: FORTY-ONE PATIENTS*

	PATIENTS WITH THYMOMA: MYASTHENIA GRAVIS	
	PRESENT	ABSENT
Tumors removed surgically	24	7
Died while in the hospital	2	1
Cause of death:		
Myasthenia gravis	2	
Pulmonary complications		1
Ineradicable tumors explored surgically: biopsy	6	4
Died while in the hospital	2	0
Cause of death:		
Myasthenia gravis	1	
Rupture of the ascending aorta	1	

*In 4 additional cases of thymoma associated with myasthenia gravis, the tumor was not explored surgically but was removed at necropsy.

operation. In the latter group, 2 were known to have had their tumors four and six years, respectively, before operation. Additional evidence of slow progression of thymomas is presented in Table III where it can be seen that of the 4 patients with ineradicable thymomas who are known to be alive, 1 has survived six months, 2 nineteen months, and 1 fifty months since operation. The duration of survival after operation for the 3 patients who had ineradicable lesions and who died after dismissal from the hospital was seventeen, forty-one and fifty-one months, respectively.

SURGICAL TREATMENT

The selection by the surgeon of the proper operative approach to a thymic tumor should be based upon a consideration of the size and location of the tumor.[15, 31, 32] For a large tumor that presents chiefly in one side of the thoracic cavity, a posterolateral, transpleural approach allows the surgeon ready access. This approach will permit the removal of large tumors that could not be easily removed otherwise. For small tumors that lie essentially in the midline, we prefer a sternum-splitting incision which provides excellent exposure of all the structures in the anterior portion of the mediastinum, and it does not necessitate entry of the pleural space. The latter advantage is shared by the transcostal or parasternal approach, but this advantage is more than offset by the inadequacy of the surgical exposure which the parasternal approach provides.

The surgical procedures carried out on the 41 patients included in our study were of three classes: removal of the tumor, removal of the tumor and the thymus, and biopsy or only partial removal of the tumor. In our experience

TABLE V. RESULTS OF THE SURGICAL REMOVAL OF THYMOMA

PRESENT STATUS	PATIENTS WITH THYMOMA: MYASTHENIA GRAVIS	
	PRESENT	ABSENT
Dead	7	1
Died in the hospital after operation	2	1
Died since dismissal from the hospital	5	0
Alive: no evidence of recurrence or metastasis	16	6
Lost to follow-up	1	0
Total	24	7

TABLE VI. PRESENT STATUS OF PATIENTS WITH THYMOMA WHO WERE OPERATED ON FIVE OR MORE YEARS AGO

	PATIENTS
Alive without evidence of recurrence	7
Alive but with evidence of progression 51 months after operation, December, 1948	1
Dead	8
Lost to follow-up	1

removal of the entire thymus together with the tumor seems to offer no advantage over the removal of the tumor alone. In the group of patients whose thymoma could be removed completely, none have died because of local recurrence of, or distant metastasis from, the tumor after being dismissed from the hospital. The results of surgical treatment of these patients are summarized in Tables III through VII.

Of the 17 patients with thymomas who were operated upon five or more years ago (Table VI), 4 had ineradicable lesions; 3 of the 4 are dead, presumably as a direct result of the tumor. The fourth patient was alive when he was last heard from in December, 1948, fifty-one months after exploration, but his condition was poor because of the existence of obstruction of the superior vena cava.

TABLE VII. ANALYSIS OF THE CAUSES OF DEATH

	PATIENTS WITH THYMOMA: MYASTHENIA GRAVIS	
TIME AND CAUSE OF DEATH	PRESENT	ABSENT
Died in the hospital after operation	8	0
Cause: Myasthenia gravis	7	0
Rupture of the aorta	1	0
Pulmonary complications	0	1
Died after dismissal from the hospital	8	0
Cause: Myasthenia gravis	4	0
Brain tumor (astrocytoma)	1	0
Unknown	3*	0

*Since these 3 patients had ineradicable tumors, death most probably was caused by the tumor as such.

Removal of a thymoma from a patient with myasthenia gravis has no evident influence on the course of the disease.[1]

RESPONSE OF THYMOMAS TO ROENTGEN THERAPY

Information bearing on the response of thymomas to roentgen therapy was available in two forms: in the size of tumors after roentgen therapy as compared to their size before such treatment, and in the histologic appearance of those tumors which had been irradiated as compared to the appearance of those which had not. Data which would permit an estimate of change in size of a tumor after roentgen therapy were available on 12 patients who had myasthenia gravis; in 10 no change was apparent; in 1 who had an ineradicable thymoma the tumor became smaller and ultimately could not be demonstrated roentgenologically, but the patient died fifty-one months after operation, presumably as a result of the tumor; and in 1 the tumor, which was observed to become smaller, was found at operation to be a fibrous-walled cyst. This latter change, however, could not with certainty be ascribed to roentgen therapy because another of our patients who had no roentgen therapy had a completely cystic lesion. Evidence of a similar nature from the patients who had thymoma unassociated with myasthenia gravis also failed to show any definite benefit to the patient from roentgen therapy.

Roentgen therapy in the doses employed for these patients had no appreciable effect upon the microscopic picture of the thymoma.

The report of Reid and Marcus[16] afforded evidence that some of these tumors are radiosensitive, that every patient with an ineradicable thymoma should be given intensive treatment.

SUMMARY AND CONCLUSIONS

Forty-five cases of thymoma in which tissue had been made available by surgical operation or by post-mortem examination form the basis of this report. We have defined a thymoma as a specific tumor of the thymus that is characterized by the presence of both thymic epithelial and thymocytic cells in varying proportions. Though this tumor is commonly associated with myasthenia gravis, only 15 per cent of the patients who have myasthenia have a thymoma, and 25 per cent of the tumors in our experience occurred in patients who had no evidence of myasthenia. For the purpose of comparative analysis the patients with thymomas were divided into two groups on the basis of the presence or absence of myasthenia. In both groups thymomas occurred almost exclusively in adults of both sexes, and symptoms due to the presence of the tumor as such were uncommon.

To attain the highest possible degree of accuracy in the roentgenologic diagnosis of thymomas posteroanterior and lateral roentgenograms and roentgenoscopy of the thorax should be employed in every patient with myasthenia gravis. Characteristically, these tumors occur in the anterior mediastinum in a position anterior to the aortic arch and the base of the heart. Some of them contain calcium in quantities sufficient to be apparent roentgenologically. Peculiar features which would permit a pathologic diagnosis on the basis of the roentgenologic findings were lacking.

Three-fourths of the thymomas in this series had a distinct fibrous capsule, but the others had broken through their capsule to invade adjacent structures: the pericardium, the pleura, the superior vena cava and the left innominate vein; and 2 spread to parietal and visceral pleural surfaces as nodular implants of tumor. No evidence was found to suggest that embolic lymphogenous or hematogenous metastasis occurred. We failed in our attempts to separate, on histologic grounds, those tumors which were invasive and those which spread by implantation, from those which were completely encapsulated.

The selection by the surgeon of the proper surgical approach should be based upon a consideration of the size and the location of the tumor.

Because of the poor general condition of 4 patients with myasthenia gravis, no surgical treatment was attempted. Of the other 41 patients, 31 underwent complete removal of the tumor and 10 underwent incomplete removal or biopsy. The cause of death of 3 of the 5 patients who died in the hospital after operation was myasthenia gravis.

In no patient whose tumor was removed completely has there been evidence of recurrence. Most of the deaths have been due to myasthenia gravis and not to the tumor itself, although in the group with ineradicable lesions, the tumor itself was usually fatal.

Thymomas cannot be regarded as innocent. Because there is no basis clinically or roentgenologically for the accurate pathologic diagnosis of mediastinal tumors, exploratory thoracotomy is indicated for all these patients whose general condition will permit.

Intensive roentgen therapy for ineradicable tumors seemed to benefit some patients.

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DISCUSSION

DR. MARK H. WILLIAMS, Binghamton, N. Y.—A thymoma may be an unexpected finding at operation. Because of the unusual x-ray findings and its deceptive gross appearance, it may be of interest to show an example of a benign asymptomatic tumor in this category, which we recently encountered in a 9-year-old boy. This tumor was discovered when an x-ray examination was made following a chest injury.

(Slide.) Among the numerous x-ray studies which were made, only these two films demonstrate a double shadow. This is seen along the right cardiac border in the posteroanterior view; it is superimposed on the heart shadow and is demonstrated to better advantage in the lateral view. Fluoroscopic examination was helpful in establishing a diagnosis. At the screen, pulsations were absent along the right border of the heart. Our preoperative diagnosis was mediastinal cyst. The tumor was approached by an incision through the right fifth interspace. At operation it appeared unquestionably to be an encapsulated lipoma; it extended over the heart anteriorly and upward over the great vessels to the thoracic inlet. After extending the incision upward and dividing the fifth and fourth costal cartilages, sufficient exposure was obtained to remove the tumor without difficulty.

(Slide.) The gross appearance of the tumor is typical of lipoma. It was much bulkier than one would expect from the x-ray findings; it weighed 255 grams.

(Slide.) The microscopic findings were surprising. Throughout this huge fatty tumor small islands of thymic tissue were found. When we went back to the gross specimen, these were readily seen as 4 or 5 mm. yellowish areas.

(Slide.) This is a recent follow-up on this boy, who was operated upon about nine months ago. He made a good recovery from the operation and has remained well.

DR. JOHN M. DORSEY, Chicago.—I should like to show slides of a patient upon whom we operated, who, I thought, had an anterior mediastinal tumor, perhaps a dermoid.

(Slide.) This shows the microscopic picture, as does the next. This tumor in the final analysis proved to be a thymoma, but I think it is well worth while to record our experience. In preoperative study, investigating diplopia as a possible symptom of myasthenia gravis with a therapeutic dose of neostigmine and finding no therapeutic response, we thought we had ruled out thymoma. The patient was given, unwittingly, curare along with pentothol during induction of anesthesia and developed respiratory arrest, necessitating postponement of surgery for a week. We should have come to the opinion immediately that this was a thymoma with latent myasthenia gravis. On removing the tumor the following week we did have a frozen section which revealed it to be a thymoma. The patient had a rather stormy postoperative course and died on the third postoperative day.

In summary, I feel that curare should be avoided in anesthesia for anterior mediastinal tumors. Immediate frozen section should be made. If they resemble tumors of thymic origin in any way, prostigmine and general supportive measures such as given myasthenics should be instituted.

DR. EDGAR W. DAVIS, Washington, D. C.—I was rather surprised to hear Dr. Seybold say, if I understood him correctly, that he could not find any definite relationship between the thymus and myasthenia gravis and that, in his opinion, the subsequent course of myasthenia gravis was not influenced by removal of the thymus gland. I should like to ask Dr. Seybold if he would care to comment on the diametrically opposite conclusions from the series of cases presented by him, which obviously have been beautifully studied, as compared with the 120 cases presented by Keynes of England. Out of Keynes' 120 cases, he reports 39 patients who are well, free from symptoms, and who do not need prostigmine, and 40 patients who are virtually well, with minimal symptoms. As I recall, Keynes' patients have been observed over a long period dating back to 1942.

DR. SEYBOLD (closing).—I should like to thank Dr. Williams, Dr. Dorsey, and Dr. Davis for their discussion. First, as to Dr. Dorsey's comments about keeping myasthenia gravis in mind in dealing with a patient who has a tumor which may be a thymoma. We have used provocative tests for myasthenia in a number of these patients. Sometimes the weakness complained of by some patients with tumor is difficult to differentiate from the specific weakness of myasthenia gravis, and it is indeed dangerous to operate on a patient with myasthenia gravis whose disease is unrecognized. It is dangerous unless it is previously recognized and the patient is adequately prepared and treated with prostigmine and other drugs that are effective.

The relation of thymic tumor to myasthenia gravis has received a lot of attention and, as we all know, within the last few years—about 1939, I believe—Dr. Blalock reported a patient on whom he had removed a thymic tumor three years before and in whom, at the time of his report, remission of the disease had followed. Since that time considerable experience has accumulated. We all know that myasthenia gravis is a remitting disease, and the efficacy of any form of treatment is difficult to assess, particularly on a short time basis. Quite recently, Dr. Eaton of our Neurological Section, who has been most interested in this problem, has published a follow-up on the patients he has been studying for eight years, and you can see from the figures I gave you in the charts that of the patients who had thymic tumors removed, approximately one-half of them are dead, and the leading cause of death was myasthenia gravis. I do not know how to account for the discrepancy between our experience which, I might add parenthetically, is in keeping with the experience of others throughout the country—the discrepancy between our experience and that of Dr. Keynes, except to say that some of these patients do seem to be benefitted for a time. But we know that myasthenia gravis, without treatment, will go into remission, and some of those remissions are essentially permanent in that they have lasted 15 or 20 years.

SYPHILIS OF THE ESOPHAGUS

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TERTIARY syphilis is a very occasional cause of obstruction of the esophagus. Being rare, it is important that every proved instance be recorded in the literature so that knowledge of the condition be increased and the profession be frequently reminded of its existence. The purpose of this paper is to report such a case and review the accumulated literature.

CASE REPORT

A 58-year-old white man was hospitalized because of difficult swallowing. Within a few days after admission he was regurgitating all food and liquids. He stated that for several years he had experienced periodic difficulties in swallowing food and liquids.

He complained of a choking sensation, tightness in the throat, and slight pain when swallowing. The laboratory examinations were not remarkable, save for highly positive Kahn and Wassermann reactions. X-ray study of the esophagus revealed a spherical tumor (Fig. 1) almost completely occluding the lumen at the cardic end. At esophagoscopy the lower end was found to be completely filled by a flesh-colored, finely irregular, nonulcerative mass. Little bleeding resulted from biopsy. Microscopic study of the specimen secured revealed only stratified squamous epithelium.

Because of the long history of dysphagia and the positive serology, it was felt worth while to give antisyphilitic therapy. The result was astounding. Relief from all substernal discomfort and from difficult swallowing was virtually complete in only a few days after the first injection of an arsenical. Continuation of the antisyphilitic treatment soon resulted in total relief of all symptoms.

Subsequent x-ray study of the esophagus (Fig. 2) showed disappearance of the tumor previously seen. Esophagoscopy was repeated sixty days after the first examination. No tumor and no abnormality were found. The mucosa at the cardiac end was normal in appearance.

The patient was discharged with instructions to continue the antisyphilitic treatment. Follow-up one year after discharge revealed that he had not received any treatment since discharge and within two months after leaving the hospital the symptoms had recurred. He did not return to the hospital.

REVIEW OF LITERATURE

Contributions to medical literature dealing with syphilis of the esophagus are rare. Guyot[1] in reviewing the literature dating from 1717 to 1930, from America, England, France, Germany, and Austro-Hungary [*sic*] found but fifty-five recorded instances. Moore,[2] in admitting that syphilis of the esophagus has a place in the literature, stated he had never personally observed a case, and that most of those patients thought to have syphilis of the esophagus were eventually found to have cancer. Guisez,[3] in over 3,000 esophagoscopies, saw only one instance of tertiary syphilis of the esophagus.

To the fifty-five cases found in the literature to 1930 by Guyot[1] he himself added two personal cases. Vezina,[4] Lukens and Ono,[5] Shimokawa,[6] Hanif,[8] Wilcox,[9] Fontana,[7] and Ponzoni[13] have each added reports of one case since 1930.

Read (by title) at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29, 30, and 31, 1949.

Glass and Freeman[10] and Avery[11] have added two cases each. Watson-Williams[14] reported four cases. Sabalette and Martinez[15] and Postigo[16] have reported one case each.

With the case which forms the basis of this paper, a total of seventy-five cases of tertiary syphilis of the esophagus have been found in the literature, twenty having been recorded since 1930.

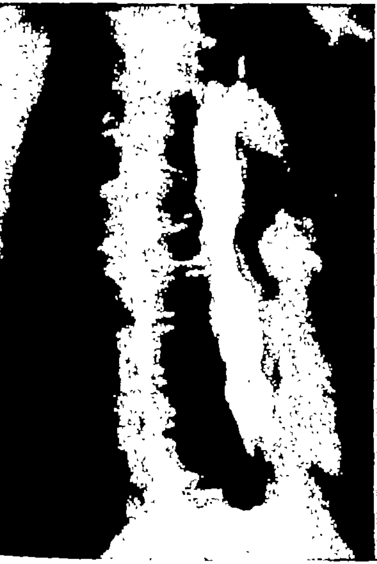

Fig. 1.

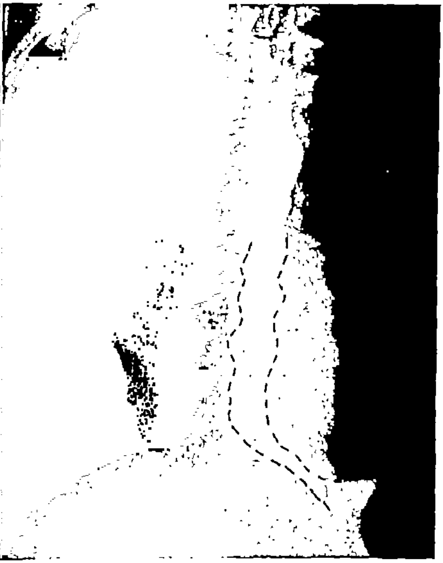

Fig. 2.

Fig. 1.—Rounded tumor mass seen obstructing flow of barium in lower esophagus.

Fig. 2.—Esophagram taken two weeks after institution of antisyphilitic treatment. Tumor no longer present and barium flows freely into the stomach.

PATHOLOGY

The gross structure of the lesion of tertiary syphilis of the esophagus may assume one of two general forms, a submucous gumma or a diffuse inflammatory reaction with destruction of tissue and resultant scarring and stenosis. Either form may display erosions and ulcerations. The gummas apparently are prone to ulceration and loss of tissue with subsequent scarring. The microscopic findings have been variously described by the few having material at their disposal. In general, the picture is that of periarteritis leading to scar formation.

SYMPTOMS

In general, the symptoms are those of obstruction of the esophagus. In addition, there may be cough, expectoration, and hemoptysis. These are symptoms of tracheal perforation.

Guyot[1] mentioned the absence of pain in tertiary syphilis as a possible differential point between this disease and carcinoma of the esophagus. Four of the patients whose cases are reviewed complained of some sort of substernal distress. All the other reports do not mention the presence of pain or specifically say no pain was present. Wile[17] stated, "Pain is not a marked symptom except during the act of swallowing. When there is ulceration, pain may be present during repose as well as deglutition. In old standing cases where scarring and consequent narrowing of the tube occur, the pain during attempted swallowing may be very severe."

The length of time of the dysphagia appears to be a fairly reliable differential symptom. In those histories in which the duration was recorded the figures were—three years, eight years, seven years, several years, ten days, six weeks, three months, two months, four months, several weeks, and eight weeks. The longer periods will, of course, eliminate esophageal cancer in any questioned case. The apparent fact that the clinical course of tertiary syphilis of the esophagus is more prolonged than that of cancer was previously noted by Myerson.[12]

X-RAY EXAMINATION

Roentgen examination of the barium-filled esophagus is of great importance in the diagnosis of any obstructive lesion. Wilcox[9] has said that the roentgenoscopic appearance of tertiary syphilis of the esophagus is more or less characteristic. He described the walls of the tube as being very rigid with little change in contour or size of the barium column as the opaque bolus passes through the stenotic area. The barium has a finely irregular outline. This is in contradistinction to carcinoma of the esophagus which, if extensive enough to produce rigidity of the wall for a considerable distance, will produce coarse irregularities with more irregular canalization. In spasm of the esophagus the outline is smooth.

ESOPHAGOSCOPY

Avery[11] stated that very few descriptions of the endoscopic findings of tertiary syphilis of the esophagus are to be found in the literature. This phase of the examination is of the greatest importance and for this reason summaries of the endoscopic descriptions of cases as they appear in the literature are presented here.

Hanif's[8] examination recorded severe injection of the mucous membrane and multiple ulceration. Guyot[1] found the esophageal wall stiff and rigid with the mucous membrane stretched and adherent. Ulcerations with sharply demarcated edges and dirty sloughs at the bases were seen. Vezina[4] reported the esophagus of his patient to show that the mucous membrane covered the granulations which bled easily. A stenosis at the cardiac end could not be passed. Fontana[7] noted ulcerations with plaques of leucoplakia nearby. The mucous membrane appeared to be involved in a "nonspecific" esophagitis with hypertrophy of the wall and dilatation of the tube above the lesion. Myerson[12] described an umbrella-like convexity of the esophageal wall which appeared intensely red and slightly swollen. The lesion bled easily.

Watson-Williams[14] reported the endoscopic findings in four patients. In the first, there was a patch of pale leucoplakia seen 3 cm. inside the esophagus. The middle one-third showed a well-marked esophagitis with patches of pale, sodden epithelium, arranged in longitudinal streaks. His second patient showed dilatation of the upper part of the esophagus. Below 27 cm. the mucosa was thickened and macerated; at 30 cm. there was a longitudinal dull streaking of the walls, apparently from denudation; at 33 cm. bright scarlet patches began to appear devoid of epithelium and bleeding on contact. At 37 cm. the whole circumference was superficially ulcerated and so contracted that only a small lumen remained. His third patient had received antisyphilitic treatment before esophagoscopy. In this case a diffuse esophagitis without special features was seen. The fourth patient showed the upper esophagus to be somewhat dilated. *The walls were flabby and in the middle third were marked with longitudinal,* streaky esophagitis.

It is reasonable to suppose that the endoscopic findings will vary a great deal with the stages at which the examinations are made. Watson-Williams described the characteristic findings at esophagoscopy as "general esophagitis tending to affect the middle two-fourths of the esophagus; maceration of the epithelium with longitudinal desquamation going on to complete shedding of the epithelium; formation of leukoplakic patches consisting of thickened epithelium only." The exact locations of the lesions in the various reports are not always given. However, the "upper end" of the esophagus was affected twice as often as the "lower end," six lesions being noted in the upper part and three in the lower part. In all of Watson-Williams' cases the middle two-fourths was given as the site of affection.

DISCUSSION

The diagnosis of tertiary syphilis of the esophagus will not often be made. In spite of this, it seems reasonable that in view of the prevalence of syphilis and the possibility that syphilitic dysphagia may occur much more commonly than is generally accepted, the condition should be thought of in the case of every patient complaining of dysphagia.

The blood serology may or may not be positive and is only of leading diagnostic significance, since an unknown number of those suffering any form of obstruction of the esophagus will have positive Wassermann and Kahn tests.

Positive biopsy findings will establish some of the diagnoses. It should be borne in mind that biopsy in the esophagus is frequently very difficult. Avery[11] felt that a history of transitory attacks of mild dysphagia is very suggestive of syphilis of the esophagus.

Guyot[1] considered as authentic cases of syphilis of the esophagus only those (a) recognized at post-mortem and (b) those found at esophagoscopy and cured by specific treatment. The diagnosis of tertiary syphilis of the esophagus should not be made on the basis alone of relief of dysphagia by specific treatment, because dysphagia may be due to gumma in the mediastinum, located in such a position as to cause partial obstruction by pressure, while not primarily involving the esophagus.

Guyot[1] mentioned the absence of pain in tertiary syphilis as a possible differential point between this disease and carcinoma of the esophagus. Four of the patients whose cases are reviewed complained of some sort of substernal distress. All the other reports do not mention the presence of pain or specifically say no pain was present. Wile[17] stated, "Pain is not a marked symptom except during the act of swallowing. When there is ulceration, pain may be present during repose as well as deglutition. In old standing cases where scarring and consequent narrowing of the tube occur, the pain during attempted swallowing may be very severe."

The length of time of the dysphagia appears to be a fairly reliable differential symptom. In those histories in which the duration was recorded the figures were—three years, eight years, seven years, several years, ten days, six weeks, three months, two months, four months, several weeks, and eight weeks. The longer periods will, of course, eliminate esophageal cancer in any questioned case. The apparent fact that the clinical course of tertiary syphilis of the esophagus is more prolonged than that of cancer was previously noted by Myerson.[12]

X-RAY EXAMINATION

Roentgen examination of the barium-filled esophagus is of great importance in the diagnosis of any obstructive lesion. Wilcox[9] has said that the roentgenoscopic appearance of tertiary syphilis of the esophagus is more or less characteristic. He described the walls of the tube as being very rigid with little change in contour or size of the barium column as the opaque bolus passes through the stenotic area. The barium has a finely irregular outline. This is in contradistinction to carcinoma of the esophagus which, if extensive enough to produce rigidity of the wall for a considerable distance, will produce coarse irregularities with more irregular canalization. In spasm of the esophagus the outline is smooth.

ESOPHAGOSCOPY

Avery[11] stated that very few descriptions of the endoscopic findings of tertiary syphilis of the esophagus are to be found in the literature. This phase of the examination is of the greatest importance and for this reason summaries of the endoscopic descriptions of cases as they appear in the literature are presented here.

Hanif's[8] examination recorded severe injection of the mucous membrane and multiple ulceration. Guyot[1] found the esophageal wall stiff and rigid with the mucous membrane stretched and adherent. Ulcerations with sharply demarcated edges and dirty sloughs at the bases were seen. Vezina[4] reported the esophagus of his patient to show that the mucous membrane covered the granulations which bled easily. A stenosis at the cardiac end could not be passed. Fontana[7] noted ulcerations with plaques of leucoplakia nearby. The mucous membrane appeared to be involved in a "nonspecific" esophagitis with hypertrophy of the wall and dilatation of the tube above the lesion. Myerson[12] described an umbrella-like convexity of the esophageal wall which appeared intensely red and slightly swollen. The lesion bled easily.

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CAVERNOSTOMY FOR RESIDUAL CAVITY AFTER THORACOPLASTY

Early Closure of Cavernostomy Sinuses Under Streptomycin Protection

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EXTRAPLEURAL thoracoplasty continues as the most commonly used major surgical procedure in the treatment of pulmonary tuberculosis. The results of thoracoplasty in terms of cavity closure vary widely in reports of different surgeons. Dolley, Jones, and Paxton[1] reported a series of 1,636 thoracoplasty operations in 1939. Among these patients 24.2 per cent were considered failures due to residual cavity and active endobronchial disease. O'Brien, Day, Chapman, and Tuttle[2] reported residual cavities in 12.98 per cent of 511 thoracoplasty patients. O'Brien[3] in objecting to routine preoperative needling of cavities, stated:

> "We have well over 1,000 thoracoplasty patients and our percentage of cavity closure will run from 80 to 90 per cent. Almost any report on a group of thoracoplasties will be the same."

Krynski[4] reported a series of 308 cases of thoracoplasty from Sea View Hospital in 1947, in which 51.3 per cent were considered arrested. The operation has become rather well standardized by several generations of thoracic surgeons and nearly all thoracoplasties now done are technically good operations. The cause of the variation in number of residual cavities reported by different authors probably lies in the selection of cases rather than in the technique of the operation. The deeper one goes in the barrel in the effort to salvage some of these questionable risks the higher will be the number of residual cavities.

At the Veterans Administration Hospital, Oteen, N. C., 525 patients have undergone a thoracoplasty in the past five years. In 20 per cent of these a residual cavity has persisted. There have been minor variations in technique in that an anterior stage was occasionally used if the cavity was in an anterior position and the processes removed or the heads of the ribs disarticulated if the cavity was proved to be in the posteromedial portion of the upper lobe. These variations have not been considered determinant factors in the number of residual cavities encountered.

The success attained in eradicating these residual cavities often determines the success of the entire surgical program. It is satisfying to obtain a negative sputum after a thoracoplasty, but it is doubly so, both to the surgeon and the patient, to attain success after an initial failure. The methods used and the results obtained in dealing with these cavities at Oteen have been described in

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another paper.[5] The insertion of a Monaldi catheter concomitantly with the thoracoplasty, as described by Vineberg and Kunstler,[6] has been used in a number of patients without alteration in the final results.

At the present time, when confronted with a postthoracoplasty cavity, resection is given first consideration. Lobectomy or pneumonectomy for residual cavity[7, 8] has been done on 44 patients at Oteen since January, 1947. The total mortality rate following these resections has been 6.8 per cent. Ninety-one and two-tenths per cent of the living patients now have a negative sputum. Wound infection, empyema, and bronchopleural fistula complicate such operations frequently *enough to act as a deterrant to unbridled enthusiasm for the method.*

Some patients, because of age, diminished pulmonary function, contralateral disease, or the size and location of the cavity, are not considered suitable risks for resection. In this group of patients we are now using open cavernostomy to obliterate the cavities. The discovery of streptomycin, in 1944, by Schatz, Bugie, and Waksman[9] and the report of its effectiveness against the tubercle bacillus in December of the same year by Feldman and Hinshaw[10, 11, 12] caused us to use this drug as an adjunct to permit early closure of the resultant cavernostomy sinuses.

The history of cavernostomy, the surgical technique employed, and the results obtained in a group of 22 patients followed for periods of four to twenty-three months are presented in this paper. Attention is given to the use of streptomycin as an adjunct to the procedure.

HISTORY

Cavernostomy, speleotomy, or open drainage of tuberculous cavities was probably the earliest form of surgical treatment used for pulmonary tuberculosis[13, 14] *and may well date back to the time of Hippocrates.*[15, 16] *The earliest* reported case of incision of a tuberculous cavity is that of Pheraeus who received a spear thrust in battle which opened a cavity in his lung and restored his health.[17] In the famous de Bligny case, the son of M. de la Genevraye, a victim of phthisis had abandoned all hope of recovery, in the year 1670, when he received a sword wound which opened a cavity in the right lung and allegedly cured his tuberculosis.[17, 18, 19]

Godlee[20] stated that Paschal, Paré, and Harvey incised the chest in desperate cases and drained tuberculous cavities. Baglivi,[21] in 1696, believed that opening a cavity led to cicatrization and advised an intercostal incision to permit the introduction of medicaments into the cavity.

Le Carboulec[10] recorded the opinions of Barry, Boerhaave, Sharpe, Pouteau, David, and Bell who opened tuberculous cavities with a lancet or trocar. According to Elliott,[22] as related by Hastings,[23] a Dr. E. Barry of Dublin,[24] in 1727, recommended puncturing tuberculous cavities as a means of curing phthisis and, in 1763, reported several cases in which he had successfully used this method. Sharpe[25] of Ireland, in 1769, recommended incising tuberculous cavities if pleural fusion had occurred and introduced a gauze drain. Bell[26] of Scotland, in 1778, referred to free incision of "abscesses" in the lung and drainage by means of lead pipes. Gumprecht[27] of Göttingen, in 1793, also advocated incision of tuberculous cavities.

In the nineteenth century, as stated by Le Carboulec,[10] incision and drainage of tuberculous cavities was attempted or performed by Ramadge (1814), Calissen (1815), Zang (1818), Nasse (1827), Krimer (1829), and Hockten (1844). About 1830, March (Dublin), according to Hastings,[22, 23] incised and drained tuberculous cavities in two patients, one of whom recovered. Hastings, however, believed the diagnosis in the successful case to be a pulmonary abscess or empyema necessitatis. About the same time Thomas of Wales performed a similar operation. In 1845, Hastings[23] reported two patients with apical pulmonary cavities in whom he procured the help of Stokes, a surgeon, to open and drain the cavities by insertion of a rubber tube. Improvement occurred in one case.

Mosler,[28] in 1873, punctured a tuberculous cavity with a trocar and cannula, widened the wound with forceps, packed it with gauze, and inserted a large silver drainage tube through which he irrigated the cavity with a dilute solution of potassium permanganate. Thereafter cavernostomy was performed with increasing frequency. Prior to 1885, incision and drainage of tuberculous cavities had been carried out by incision, or insertion of a trocar and cannula, through an intercostal space without resection of any portion of the thoracic cage. In the development of cavernostomy and in the advancement of thoracic surgery much credit is due de Cérenville of Lausanne, Switzerland, because he not only performed the first thoracoplasty for pulmonary tuberculosis, but combined this procedure with cavernostomy. In 1885,[29] he reported four cases of pulmonary apical cavities in which he resected portions of the second and third ribs anteriorly and in two opened the cavities intentionally. For postoperative dressings he used gauze, cotton, iodoform tampons, alum, thymol, balsam, and caustic agents. Improvement, however, was only temporary.

In 1891, Sonnenburg[30] reported his famous case of cavernostomy in which, under Koch's direction, he resected the first rib and cartilage, opened into the cavity with thermocautery, and injected tuberculin into the wound which was packed with gauze. The result was remarkable and the patient was well five years after operation. Tuffier,[31] in 1944, collected 45 cases of cavernostomy. Seventeen of these terminated fatally within three months after operation. He concluded that Sonnenburg's case was the only one with an incontestable favorable result.

In the second decade of the twentieth century Sauerbruch of Germany contributed greatly to the development of cavernostomy. In 1920,[32] he presented the theory that a reduction in the size of the thoracic cage should be obtained prior to cavernostomy, either by a preliminary thoracoplasty or by extrapleural pneumonolysis or both. In his publication in 1930,[14] he described the technique of resection of portions of the overlying ribs. The cavity was then entered by incision or cautery and packed with gauze. He also stated that after two or three months a soft tissue plastic operation could be performed to close the fistula.

Cavernostomy was of interest to European surgeons for many years prior to its introduction in the United States. It was not until 1924 that Gekler, Rankin, and Weigel[33] reported three cases of cavernostomy in which postoperatively gentian violet and methylene blue were instilled into the cavities to produce chemical sterilization, with favorable results. Lilienthal, in 1927[34] and 1929,[35] reported a total of four cases of cavernostomy for residual cavity after thoracoplasty and in 1931,[36] reported two additional cases in which he inserted a pedicled muscle flap into the cavity, thus applying the original method devised by Pool and Garlock[37] for closure of persistent bronchial fistula. He reported success in one instance and failure in the other. Bruns and Casper,[38] in 1932, reported 22 cases of cavernostomy with disappointing results. In 1935, Eloesser[39] devised his U-shaped skin flap technique for drainage of tuberculous empyema and shortly thereafter he and others adapted this technique to cavernostomy. In 1937, Neuhof[40] advocated closure of residual bronchocutaneous fistula after cavernostomy by means of a fat transplant when simple plastic repair failed. Alexander,[41] in 1937, mentioned the use of a pedicled muscle graft to close residual bronchocutaneous fistula.

Up to comparatively recent years cavernostomy has been fraught with so many dangers, difficulties, and poor results that none of the many surgeons who have attempted it have continued to use it as a standard procedure. Revival of interest in cavernostomy came along with new concepts or theories as to the mechanics and aerodynamics of formation and closure of cavities. Hall,[42] in the British Isles in 1922, after study of pathologic specimens, first called attention to the importance of the condition of the bronchus draining a cavity and described a flap valve mechanism. Ameuille and Levesque (1923),[43] Eloesser (1934),[44] and Korol (1935)[45] also emphasized the importance of the state of the connecting bronchus. Coryllos,[46] in 1936, made a meritorious contribution when he postulated that changes in the size of cavities and their closure or resistance to healing were due to the state of the connecting bronchial openings. He and Ornstein[47] acted on the theory that the cavity would close if the draining bronchus was obliterated. They attempted this obliteration by (1) an intracavitary transthoracic injection into the cavity of various substances, (2) cauterization of the bronchial openings through a cavernoscope, and (3) intracavitary transplantation of a pedicled muscle flap. The report of their results in 1938 was not encouraging.

Eloesser,[48, 49] Salkin, Cadden, and McIndoe,[50] Shipman,[51] Pinner,[52] Auerbach and Green,[53] Brunn, Shipman, Goldman, and Ackerman,[54] Goldman,[55] Shipman, Rogers, and Daniels,[56, 57] and others recognized the important role of the draining bronchus in "tension cavities," but disagreed as to the necessity of closing the draining bronchus to bring about closure of the cavity. They recognized the fact that other factors, termed by Eloesser as extrinsic, also played a role in the formation and closure of cavities. Other authors also contributed to our modern understanding of cavity mechanics. Among these are, Pearson,[58] Brooke,[59] Ameuille, Delhomme, and Raust,[60] Loesch,[61] Thomas,[62] Meyersburg, Gruber, and Lupo,[63] Riggins and Gearhart,[64] Maier,[65] LeCarboulec,[18] Vineberg and Kunstler,[6] Bernou,[66] Bobrowitz,[67] Brock,[68] and Even and Lecoeur.[69]

Among the most detailed studies of cavernostomies in recent years have been those of Le Carboulec,[18, 70] Hochberg, Fink, and Chardack[71] and O'Brien, O'Rourke, Test, and Skinner.[72] Le Carboulec used the operation only for residual postthoracoplasty cavities and emphasized the necessity of weekly postoperative cauterization of the walls of the cavity and the bronchial orifices. He stated that contrary to some other authors he had always found several bronchial openings communicating with the cavity. The purpose of the cautery in his opinion is not to obliterate the bronchial orifices and achieve cure by atelectasis but to destroy the tuberculous focus at its site. By relieving the cavity of its caseous burden it then is permitted to heal by swelling and contraction of its walls. In his series of 21 cases there were two operative deaths. Among the 19 survivors, 13 had a negative sputum and a healed wound. In 6 patients a sinus persisted or there was an ipsi- or contralateral exacerbation of disease. The average duration of drainage in the healed cases was 12 months. The author stressed the fact that cavernostomy should be used only in postthoracoplasty cavities in whom the cavity represents the sole remaining focus of disease.

In 1945, O'Brien and associates reported a group of 74 patients upon whom they had performed a cavernostomy. Among these were 13 patients who had a residual postthoracoplasty cavity. Fifty-five per cent of the 11 patients who survived in this group were reported as healed and arrested. Nine per cent were improved, 9 per cent unclassified and 27 per cent dead. Among the living patients of the entire series who had been operated on earlier than one year prior to the preparation of the report wound healing occurred in 56 per cent. These authors did not use the skin flap technique.

TECHNIQUE

The operation is performed in two or more stages. The cavity is first localized with posteroanterior and lateral x-ray films. A lead marker is fixed to the skin in the subclavicular and midaxillary area before exposure to aid in localization. Planigrams are also taken to determine the level of the cavity and for comparison in the postoperative determination of cavity closure. In most cases the best site for approach to the cavity has been found to be the midaxillary region.

FIRST STAGE

The first stage is performed under general anesthesia. A U-shaped flap of skin is raised with the free end distally. The flap is made long enough to permit insertion of the free end into the cavity when it is opened at a later date. Excess fatty tissue is removed. Regenerated ribs and muscle bundles overlying the cavity are excised over a wide area. The parietal pleura is exposed by dissection with small "bronchial sponges" and as large an extrapleural space as possible developed. The free end of the skin flap is then tucked into the wound which is packed with plain gauze. A metal skin clip is fixed to the end of the gauze packing and placed at the projected site of the cavernostomy. This serves as a guide to the best approach to the cavity when later x-ray studies are made. The wound is then closed as tightly as possible around the skin flap with interrupted chromic No. 1 sutures for the deep tissues and nylon sutures for the skin.

SECOND STAGE

The second stage is performed 10 to 14 days later. There is occasionally a moderate amount of seropurulent drainage from the wound during this interval. Local anesthesia is used for the second stage in order to preserve the cough reflex and aid the patient to expel any blood or pus that might enter the bronchial tree. The wound is reopened and the pack removed. The site of the skin clip is noted and compared with x-ray films to aid in localizing the cavity. Pleural fusion is first assured by needle aspiration. An attempt is then made to enter the cavity with an 18-gauge needle attached to a syringe. It is wise to sound a note of caution at this point. Following a thoracoplasty the superior portion of the upper lobe is compressed to a narrow tongue of tissue which extends upward between the mediastinum and the collapsed chest wall. On the left side the aorta must be avoided as well as the subclavian vessels. On the right side the azygos vein and the superior vena cava are endangered. When the cavity is entered, manometric readings are taken before and after injection of 10 c.c. of air through the needle and following withdrawal of 20 c.c. of air. These readings serve as an indicator as to whether or not we are dealing with a blocked cavity. If the bronchus draining the cavity is open the pressure readings will not be altered by introduction or withdrawal of air. If the cavity is blocked by a valve the readings will be elevated to +8 to +14 on introduction of 10 c.c. of air. When 20 c.c. of air is then withdrawn readings of –3 to +3 are obtained. As large an area of the cavity as possible is then unroofed. This may be done by the electrocautery blade or, if the large vessels are threatened, by sharp dissection. The distal end of the skin flap is then sutured to the cavity wall with mattress sutures of chromic No. 1 gut and a gauze pack placed into the cavity and wound to hold the flap in place. If the site is too inaccessible the sutures are omitted and the gauze pack relied upon to hold the flap in situ. We have often failed to locate the cavity at this stage and have then repacked the wound and made further x-ray studies before finally entering the cavity.

POSTOPERATIVE CARE

If the cavity is successfully entered the pack is left in place for four days. It is then removed and the sinus packed daily with gauze moistened with an antiseptic solution. Formerly we used one composed of equal parts of penicillin (250 units per c.c.) and a 1 per cent solution of acetic acid. At present we are using Chloresium. This regime has kept the wound clean and free of pyocyaneus infection which we occasionally encountered prior to its use. Penicillin is administered intramuscularly for a few days before and after each stage until the temperature reaches the normal level. It is necessary to gently dilate the cavity stoma with the gloved finger at weekly intervals in order to prevent too rapid contraction of the opening.

CLOSURE OF THE CAVERNOSTOMY

After a period varying from three to five months the drainage usually becomes thin and scanty. The sinus tract narrows and epithelializes. The

TABLE I

CASE NO.	CAVITY		STREPTOMYCIN		RESULTS			COMPLICATIONS	MONTHS SINCE CLOSURE
	OPENED	CLOSED	BEGAN	ENDED	CAVITY	SINUS	SPUTUM		
F. B. 1	1-26-46	3-14-47	2-28-47	3-28-47	Equivocal	Closed	Neg.	None	24
F. R. 2	8-21-46	—	—	—	—	—	—	Traumatic pneumothorax, contralateral spread, died 26 days postop.	—
Z. S. 3	11-25-46	5-13-47	4-12-47	8- 7-47	Closed	Closed	Neg.	None	22
J. W. 4	12-13-46	4- 9-47	3-25-47 4-30-47	4-23-47 5-19-47	Closed	Closed	Neg.	None	23
E. J. 5	1-22-47	5-13-47	4-11-47	6-13-47	Closed	Closed	Neg.	Traumatic pneumothorax, 2nd stage, re-expanded	22
C. P. 6	2-24-47	5-15-47	4-17-47	6-12-47	Closed	Closed	Neg.	None	22
S. R. 7	2-24-47	6-20-47	5-24-47	8-10-47	Closed	Closed	Neg.	None	21
J. B. 8	3-12-47	7-25-47	6-25-47	9-22-47	Open	Open	Pos.	Primary healing, late recurrence	13
E. B. 9	5- 5-47	8-22-47	7-21-47	10-10-47	Closed	Closed	Pos.	Late contralateral cavitation	19
D. L. 10	5- 5-47	10- 8-47	9- 2-47	11-20-47	Closed	Closed	Neg.	Traumatic pneumothorax, 2nd stage, re-expanded	17
J. P. 11	6- 4-47	9-18-47	8-14-47	10-24-47	Closed	Closed	Neg.	None	18
C. J. 12	8-28-47	3- 3-48	2- 4-48	4- 5-48	Closed	Closed	Neg.	None	13
W. P. 13	9-12-47	4- 2-48	3- 2-48	5- 4-48	Closed	Closed	Neg.	None	12
T. P. 14	10-15-47	4- 5-48	3- 2-48	5- 4-48	Closed	Closed	Neg.	None	12
O. P. 15	10-24-47	—	—	—	Open	Open	Pos.	Contralateral reactivation	—

R. L. 16	12- 5-47	4- 6-48 7-12-48 9- 3-48	4- 7-48	8- 3-48	Closed	Intermittent drainage	Neg.	Persistent sinus	7
A. Y. 17	4- 6-48	11- 1-48	10-28-48	11- 7-48	Closed	Closed	Neg.	None	6
T. T. 18	4- 6-48	—	—	—	Open	Open	Pos.	Ipsilateral basal cavitation	—
W. L. 19	5-12-48	10-29-48	10-27-48	11-12-48	Closed	Closed	Neg.	None	5
W. S. 20	9-27-48	—	—	—	Open	Open	Pos.	Late hemoptysis	—
K. S. 21	11- 5-48	—	—	—	Open	Open	Neg.	Ipsilateral pleural effusion, late	—
J. G. 22	12- 9-48	—	—	—	Open	Open	Pos.	Traumatic pneumothorax, 1st stage, re-expanded	—
W. P. 23	2-21-49	—	—	—	Open	Open	Neg.	None	—

sputum is studied by concentration and culture and the sinus secretions by culture for acid-fast organisms. If three successive cultures of both the sputum and drainage material are negative and planigrams indicate an eradication of the cavity, closure is attempted. Our present policy is to administer a 1 Gm. daily dose of streptomycin for one week preoperatively and two weeks postoperatively. This is divided into two doses of 0.5 Gm. each.

Under general inhalation anesthesia given through an intratracheal catheter, the skin flap is freed and the sinus tract excised. As much regenerated bone as possible is again removed from around the sinus and a pedicle graft developed from the edge of the pectoralis minor muscle. The free end of the graft is fixed in place at the site of the previous cavity by mattress sutures of No. 1 chromic gut. The excess skin flap is excised and the wound closed with interrupted chromic No. 1 sutures for the deeper structures and nylon for the skin.

COMPLICATIONS

Traumatic pneumothorax occurred during four operations. One patient died, the others re-expanded, and the operation was later completed. Reactivation of disease occurred in 3 patients. One was the patient who died. He had a moderate contralateral reactivation at the time of death. Another patient developed a second cavity in the lower lobe some distance posterior to the original cavity which had been drained anteriorly. The posterior cavity was opened from a posterior approach. The third is clinically improved although the sinus has not been closed.

RESULTS

The results of the entire series are given in Table I.

The combined results are given in Table II.

TABLE II. RESULTS OF CAVERNOSTOMY SERIES

CAVITIES OPENED	CAVITIES CLOSED	DEATHS		SPREADS		NEGATIVE SPUTUM IN CLOSED SINUSES		RECURRENCE IN CLOSED SINUSES	
		EARLY	LATE	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
23	16	1	0	2	8.7	13	81.2	2	12.5

Twenty-three patients with residual postthoracoplasty cavities have had their cavities drained by an open cavernostomy. Sixteen have had the resultant sinus tract closed by a muscle plastic operation, using streptomycin as an adjunct. Thirteen of these have been closed and followed for periods varying from one to two years.

One patient died following the first stage operation. Traumatic pneumothorax was incurred at the operation and a contralateral spread followed. Death occurred suddenly on the twenty-first postoperative day, apparently of a pulmonary embolism.

Seven patients still have a draining sinus. Three of these are recent cases and will ultimately be closed. The remaining three were poorly selected cases and cannot be closed. The prerequisite established by Le Carboulec that the cavity must represent the sole remaining focus of disease was not followed. One of these patients had caseous disease in the entire lung and although the cavity has apparently been eradicated a pneumonectomy will ultimately be required. One patient has required a second drainage of another cavity in the same lung. He has shown dramatic clinical improvement and recently had a negative concentrated sputum for the first time in five years. The third patient represented a salvage attempt. A giant cavity occupied an entire lung in a patient with extreme toxic symptoms. A Monaldi drainage was followed by a thoracoplasty and finally an open cavernostomy. He also has shown dramatic clinical improvement. Contralateral cavitation is being controlled. No effort has been made to close the sinus.

Sixteen patients had the sinus closed by a muscle plastic operation. In three patients, tissue sections of the excised skin flap were made at the time of closure. The findings of Coryllos[47] were confirmed in these for typical tubercles were found in the section. All wounds except one healed by primary intention or after one to two weeks of drainage. In one patient, despite three attempts at closure a small sinus continues to drain intermittently. One patient whose wound had healed by primary intention had a recurrence of the sinus and a positive sputum thirteen months later. A bilobectomy was then done and the patient now has a healed wound and a negative sputum.

Thirteen of the patients whose sinuses were closed have a negative sputum. The patient with the persistent sinus has an occasional positive sputum. The patient with the persistently positive sputum obtained a successful result following the cavernostomy. He had a negative sputum for several months following closure. He is an alcoholic, however, and ultimately developed a contralateral cavity. The patient who had a lobectomy for recurrent cavity and positive sputum now has a negative sputum.

The residual cavity has been definitely eradicated, as revealed by planigraphic x-ray studies in 12 of the 16 patients whose sinuses were closed. Three of the remainder have planigraphic x-ray studies consistent with bronchiectasis in the former cavitary area. Two of these have a consistently negative sputum nearly two years after closure. One definite recurrence of sinus and cavity required lobectomy.

CONCLUSIONS

1. The technique of cavernostomy in a consecutive series of 22 patients who had a residual cavity after thoracoplasty has been presented.

2. The use of streptomycin as a protective agent in surgical plastic closure of cavernostomy openings in 16 patients has been discussed. Streptomycin has made possible the early closure of sinuses resulting from cavernostomies with complete healing of 93.7 per cent of 16 attempts.

3. Cavernostomy with streptomycin as an adjunct offers a satisfactory form of treatment for patients with residual cavities who are not suitable risks for resection.

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DIAPHRAGMATIC HERNIA

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INTRODUCTION

IN THE past decade outstanding articles have appeared in the literature on diaphragmatic hernia. It is a condition which nowadays is diagnosed clinically with greater frequency than it was some twenty to thirty years ago. Harrington, Hedblom, Truesdale, Ladd and Gross, Marks, Donovan, and Sweet have contributed much in American literature on this subject.

Historically Paré, in 1579, reported the autopsy findings in a case of diaphragmatic hernia caused by trauma. Cooper reported several cases in 1798. Between 1856 and 1920, Rowlands found only two cases in the records of Guy's Hospital in London.

EMBRYOLOGY

The development of the diaphragm and the descent of the stomach, as well as the formation of the pleural and peritoneal cavities, makes the diaphragm susceptible to weak areas through which hernias may occur. They may be present at time of birth or may develop later on in life.

The complex separation of the celomic cavity into pleural, pericardial, and peritoneal cavities begins in the 2.1-mm. embryo. It is completed in the 20-mm. embryo. If a hernia of a portion of the gut occurs before this division is completed, the loops of bowel will not be covered by serous membrane. The hernia would not be a true one. If the hernia occurs after the serous cavities are formed but before the muscular elements of the diaphragm have completely fused, the bowel would be covered by serous membrane. It would then be a true hernia. The communication between the pleural and peritoneal cavities closes in the third month of intrauterine life.

The muscle fibers that grow in between the pleural and peritoneal cavities are derived from the third and fourth cervical myotome, while in the cervical region.

The anterior, lateral, and central portions of the diaphragm develop from the septum transversum and the fused ventral mesentery.

The posterior, lateral, and central portions of the diaphragm are formed by the fusion of the dorsal mesentery and mesoderm with the pleuroperitoneal membrane. This membrane is derived from the pulmonary ridge. Unilateral absence of the diaphragm is probably due to failure of development of the pleuroperitoneal membrane. It is then found as a narrow ridge of tissue along the posterior wall of the thorax.

The mesodermal cells derived from the receeding Wolffian body form the right and left crura of the diaphragm.

Read (by title) at the Twenty-eighth Annual Meeting of The American Association for Thoracic Surgery, Quebec, Canada, May 31, June 1, 2, 1948.

The dorsal mesentery forms the posterior and central portions of the diaphragm. This portion contains the esophageal hiatus.

The pleuroperitoneal membrane grows ventrally. It closes the remaining opening, namely, the pleuroperitoneal hiatus between the pleural cavity and the peritoneal cavity. This closure occurs by fusion between the pleuroperitoneal membrane and the septum transversum. This forms the lateral portion of the diaphragm. The hiatus closes in the 17- or 18-mm. embryo on the right side, and in the 19- or 20-mm. embryo on the left side.

If the mesoderm is not properly deposited at any of these adjacent points of union, or if there is failure of proper fusion, it may result in the congenital continuity of the pleural and peritoneal cavities; or it may result in congenital weak points in the diaphragm. These weak points would occur at points of fusion of the previously named structures.

These weak points would be at:

1. Foramen of Bochdalek—pleuroperitoneal hiatus situated dorso-laterally.
2. The outer crus.
3. The esophageal hiatus.

The stomach descends behind the septum transversum. It should have reached its permanent site before the left half of the diaphragm is closed. If there is a delay in the descent of the stomach, the lumbar portion of the diaphragm will not have developed perfectly and the esophageal hiatus will have developed around the cardia of the stomach instead of around the esophagus. This results then in an unusually large esophageal hiatus. There will be a deficiency in both the muscle ring and in the attachments of the diaphragmatico-esophageal membrane. The abnormal position of the stomach will cause the widening of the esophageal hiatus and a wide space between the margins of the muscle and the wall of the esophagus. It will also cause improper fixation of the elastic membrane between the muscle margin and the stomach and esophagus as well as an abnormally large peritoneal fold extending well down on the cardia of the stomach.

The more defective the development of the esophageal hiatus the greater are the chances that an esophageal hiatus hernia may develop later on in life.

The dome of the diaphragm is not a fusion region. Therefore, any hernias that occur through this portion of the diaphragm cannot be attributed to embryologic development. It must be due to either degeneration of the muscle or some other pathologic condition or injury.

Embryonic and congenital hernias are, however, the result of improper development of parts of the diaphragm. Persistence of the dorsopleural recess may be a factor in the origin of these hernias.

All of these factors explain the fact that diaphragmatic hernias are more common on the left side than on the right side.

ANATOMY

The diaphragm is composed of three parts which insert into a central tendon. These parts are:

1. The sternal portion.

2. The costal portion.
3. The lumbar portion.

The sternal portion arises from the xiphoid process. The costal portion arises anteriorly and laterally from the six lower ribs. The lumbar portion arises posteriorly from the crura and from the two lumbocostal arches.

The crura arise from the first three lumbar vertebrae.

The medial lumbocostal arch of Haller is a fibrous band which extends from the body of the second lumbar vertebra to the tip of the first lumbar transverse process. Under this arch passes the psoas muscle. The lateral lumbocostal arch of Haller extends from the tip of the first lumbar transverse process to the twelfth rib. The quadratus lumborum muscle passes under this arch.

Even in a normal adult there may be a triangular space which separates the muscle fibers of the outer crura of the lumbar portion and the last muscular portion of the costal portions of the diaphragm. This space is filled in by a thin layer of connective tissue, the continuation of the iliac fascia, which is covered above by pleura and below by peritoneum. This layer of connective tissue is less elastic than the surrounding fibers and, therefore, may be more easily torn. This area is protected by the liver and by the fatty tissue surrounding the adrenal and kidney on the right, or else it would more often be the site of hernias. It explains the fact that 95 per cent of all hernias occur on the left side.

Failure of fusion of the lumbar and costal portions in children results in a persistent hiatus in this triangular space or the hiatus pleuroperitonealis. This was described in 1848 by Bochdalek and, therefore, is commonly called the foramen of Bochdalek. The apex is curved toward the central tendon upward and forward. The base is turned downward and somewhat backward and partly rests on the twelfth rib. The borders of the foramen are muscular and are of a somewhat sphincter-like construction.

The inner crus of the diaphragm is separated from the middle crus by slits through which pass:

1. The greater and lesser splanchnic nerves.
2. The vena azygos major on the right, although it may pass through the aortic opening.
3. The vena azygos minor on the left.

These are not sites for hernias.

If there is a failure of fusion of the sternal portion with the costal portion of the diaphragm, an opening exists to either side of the xiphoid process. This opening is filled in with areolar tissue and is covered above with pleura and below with peritoneum. The deep epigastric vessels pass through this space. These openings are called the foramina of Morgagni or Larrey's spaces.

The diaphragm and transversus abdominis muscle are continuous with one another. This can be readily demonstrated by separating them from the costal arch. This converts the two muscles into a continuous fibromuscular sheet with a common aponeurosis. With the rectus sheath and the lumbar fascia this sheet encloses the abdominal cavity (Rives and Barker). The diaphragm is continuous with the inner fibromuscular layer of the abdominal wall.

There are several openings in the diaphragm through which important structures normally pass:

1. Aortic opening.
2. Opening for the vena cava.
3. Esophageal hiatus.

The aortic opening is actually behind the diaphragm at the level of the first lumbar vertebra. The crura form the lateral boundaries as they extend forward from their origin on the anterior aspect of the spine. The opening is bounded by dense fibrous tissue. The azygos vein and the thoracic duct pass through this opening close to the aorta. No hernia has ever been known to occur through this opening.

The vena cava opening is higher and more anterior on the right side. It is at the level of the intervertebral disc between the eighth and ninth vertebrae. It lies within the central tendon and is protected by the liver. It is not the site of hernias.

The esophageal hiatus is more anterior than the aortic opening and is at the level of the tenth thoracic vertebra. It transmits the esophagus, the esophageal vessels, and the vagus nerves. It lies entirely within the muscular portion of the diaphragm. It is surrounded by decussating muscle bundles of the crura before they spread out and insert into the central tendon. The size of the opening varies greatly. The muscle bundles of the hiatus are innervated by the left phrenic nerve. It is normally situated to the left of the midline.

The muscle fibers of the hiatus are only loosely approximated to the lower end of the esophagus and are not directly attached to it. The diaphragmatico-esophageal membrane brings about the fixation of the diaphragm to the lower end of the esophagus and the upper end of the cardia. It is inserted into the lower 2 to 3 cm. of the esophagus and the upper 1.5 to 2 cm. of the stomach in a fanlike manner. It is composed of elastic and fibrous tissue.

The membrane allows a certain amount of mobility between the diaphragm, esophagus, and cardia during swallowing and respiration. It acts as an antagonist to the longitudinal muscle fibers of the esophagus which tend to pull the cardia through the hiatus.

The abdominal portion of the esophagus is loosely covered to the left and anteriorly by peritoneum. The uppermost portion of the stomach is loosely covered by peritoneum for 2 cm. anteriorly and 3 cm. posteriorly. Here the peritoneum fuses with the serous covering of the stomach. The union of these two folds forms the gastrophrenic ligament which fixes the cardia of the stomach to the diaphragm. The ligament continues to the left to form the phrenico-colic ligament. Under this loose peritoneum is a fat pad. This loose peritoneal attachment allows free motion of the esophagus without traction on the peritoneum (Harrington).

CLASSIFICATION

There is no universally accepted classification of diaphragmatic hernia. The two best classifications are the one by Harrington and the one by Marks.

Harrington classifies the hernias into:

1. Nontraumatic.
2. Traumatic.

The nontraumatic hernias are again divided into:

1. Congenital—at birth.
    a. through foramen of Bochdalek
    b. esophageal hiatus
    c. through foramen of Morgagni
    d. through absence of the diaphragm
2. Acquired after birth.
    a. through esophageal hiatus—with sac
    b. through region of the fusion anlages of the diaphragm
    c. through the sites of congenital hernia

The traumatic hernias are divided into:

1. Indirect—by crushing injury.
    a. at any point of the diaphragm
    b. through the esophageal hiatus—usually with sac
    c. through the leaf of the diaphragm—usually no sac
2. Direct.
    a. by missile or knife
    b. rupture due to
        1. necrosis—abscess below diaphragm
        2. inflammatory necrosis in empyema with pressure necrosis of drainage tube usually in the posterior diaphragm with no sac.

Marks's classification is also a useful one. It is based on his findings in x-ray studies of 29 cases over a period of two and one-half years. He bases it on whether the cases are amenable to surgical repair or not.

His classification is:

1. Thoracic stomach with very short esophagus and entire stomach above the diaphragm.
2. Diaphragmatic hernia with short esophagus, part of the stomach above the diaphragm.
3. Hiatus hernia—esophagus of normal length, hernia through hiatus composed of stomach, possibly the colon.
4. Congenital hernia—
    a. through the foramen of Bochdalek
    b. through the foramen of Morgagni
    containing large and small bowel, frequently with other organs.
5. Congenital absence of diaphragm.
6. Eventration of diaphragm.
7. Traumatic hernia.

The type of hernias that require surgical intervention are:

1. Esophageal hiatus hernia.
2. Traumatic—direct or indirect, inflammatory, or necrosis of the diaphragm.

3. Absence of the diaphragm.
4. Hernia through the hiatus pleuroperitonealis—foramen of Bochdalek.
5. Hernia through the foramen of Morgagni.

Signs of hernias that require surgical intervention are:

1. Cases in which the stomach alone is involved. When these hernias get bigger, the omentum and colon also enter the hernia as well as the spleen.
2. Cases in which multiple organs are involved as the traumatic or congenital hernias. The symptoms may become more varied and severe, and there may be development of obstruction or severe hemorrhage.

THORACIC STOMACH

Bailey described this condition in 1919. It is not acquired but is a congenital abnormality. It is not amenable to surgery. All or nearly all of the stomach is above the diaphragm, fixed by reason of an extremely short esophagus. It is really not a hernia. The stomach never was in a normal position. To be a hernia the organ must have been in a normal position and then shifted into an abnormal position. The esophagus enters the top of the stomach and may be only three inches long. The pylorus lies at the hiatus, above or just below the diaphragm. The esophagus may end at the level of the fourth thoracic vertebra.

DIAPHRAGMATIC HERNIA WITH SHORT ESOPHAGUS

1. The stomach is surrounded by a serous sac.
2. The esophagus ends at the level of the seventh or eighth thoracic vertebra.
3. The stomach is in the posterior mediastinum.
4. It is important to differentiate as surgical repair is possible but is very difficult.
5. The difference between normal and abnormal length of the esophagus may be only a matter of centimeters.
6. The upper end of the stomach looks like a dilated esophagus, and there is no evidence of a rounded fundus.
7. The esophagus enters the stomach at the uppermost portion.
8. In a true hiatus hernia the esophagus is not shortened but is tortuous. The entrance into the stomach is to one side or other, not in the midline at the apex of the stomach.
9. The hiatus hernia is sometimes only seen on x-ray examination with the patient recumbent, supine, or in Trendelenburg posture. In a shortened esophagus the stomach is at all times within the chest even with the patient erect.
10. The stomach must remain at all times partially within the chest.
11. A hiatus hernia is only visualized in the erect posture if large or if the structures are adherent.
12. Frequently, a stricture is present at the junction of the esophagus with the stomach, and there may be some difficulty in swallowing.
13. A shortened esophagus may be treated surgically in some instances.

14. Harrington has reported cases in which the left diaphragm was paralyzed and the hiatus could then be closed around the esophagus above the stomach. It depends a great deal upon the symptom complex whether surgical repair should be contemplated and undertaken.

HIATUS HERNIA

The esophageal hiatus hernias may be divided into:

1. Small hernias with the pouch of herniated stomach alongside the esophagus, the so-called paraesophageal hernias. The esophagus is below the diaphragm. *These cases formed one-third of all the patients operated on by* Harrington.

2. Large hernias in which the esophagus lies above the diaphragm but is not short. The stomach extends into the mediastinum and may fill the mediastinum or it extends either into the left chest or possibly the right chest. These cases formed two-thirds of the cases operated on by Harrington.

3. Very small pulsion types of hernias due to the incompetency of the hiatus. This occurs in older persons due to atrophy of the diaphragmatico-esophageal membrane.

With younger persons, if the hiatus is abnormally large, a hernia may develop with increased intra-abdominal pressure, respiratory difficulties, or by trauma. In older persons with abnormally large hiatus and with atrophy of the diaphragmatico-esophageal membrane hernias may develop. These belong to Group 3 above.

In the smaller types of hernia the elastic membrane forms one of the coverings of the hernial sac. In larger hernias the membrane is pushed forward and the hernial sac enters the posterior mediastinum without any barrier. The loose peritoneal fold fuses with the stomach serosa farther down than normal in true hernias. The peritoneal fold and the gastrophrenic ligament join the cardia of the stomach in an abnormal manner when the hiatus muscular ring is abnormally enlarged. These hiatus hernias, therefore, are probably the result of delayed descent of the esophagus in relation to the development of the lumbar portion of the diaphragm.

The smaller hiatus hernias may turn into the larger hernias similar to other types of sliding hernias. Occasionally, the lower end of the esophagus may dilate.

Hiatus diaphragmatic hernias are the most common type. They must constantly be considered in the differential diagnosis of upper abdominal pathology. The large hiatus hernias must be differentiated from the thoracic stomach with a short esophagus. If a good part of the stomach passes up through the hiatus, the gastrocolic omentum may drag a portion of the colon up with the stomach into the hernial sac. The stomach may frequently be inverted. It usually lies to the left of the midline. The intrathoracic portion usually rotates with the axis passing through the cardia so that the greater curvature lies cephalad.

Symptoms.—These may be vague. The size of the hernia does not have much relation to the symptoms. Small hernias may give severe symptoms.

The symptoms may depend on the time of examination and the stage and size of the hernia. Ohler and Pitko have described a hiatus hernia syndrome:

1. Feeling of pain, fullness, or distress in the epigastrium and under the tip of the xiphoid coming on at the beginning of a meal. It may be so severe that the patient has to stop eating.
2. When the patient gets up and walks about the symptoms suddenly disappear and the patient can continue eating the meal.

This syndrome practically permits a diagnosis of a hiatus hernia. Cardiospasm and esophageal diverticulum can give similar symptoms on beginning a meal, but when the patient walks about the symptoms do not disappear as quickly.

The coexistence of other intra-abdominal conditions must constantly be kept in mind. There is a high incidence of coexistence of duodenal diverticulum and colon diverticulosis. Weintraub and Tuggle in 310 cases of duodenal diverticulum found a coexistence of 9 per cent of hiatus hernia and 23 per cent of colon diverticulosis.

Pain, distress, eructation, vomiting, dyspnea, heart palpitation, and weakness are frequent symptoms. These symptoms may be very severe with pain radiating down the left arm. Some of these symptoms may be caused by pressure on the vagus nerve in the esophageal hiatus. These symptoms may be relieved as mentioned previously in the syndrome findings by assuming the upright position or by lying down, by soda bicarbonate, by induced vomiting, by belching, or by defecation. Hemorrhage with secondary anemia are complications which are quite common. Erosions, ulcers, and varicosities of blood vessels occur in the herniated portion of the stomach.

Differential Diagnosis.—The main diseases from which hiatus hernia must be differentiated are:

1. Gastric or duodenal ulcer.
2. Cholecystitis with or without cholelithiasis.
3. Hyperacidity or secondary anemia.
4. Cardiac disease, especially angina pectoris.
5. Carcinoma of the cardia, stricture and diverticulum of the esophagus.
6. Appendicitis.
7. Intestinal obstruction.

One must constantly be conscious of the possibility of the presence of a hiatus hernia in addition to any one of the preceding conditions.

Physical Signs.—In small or medium hiatus hernias physical signs are absent. Only in the large hernias are signs present and then may be present or absent at various times of examination. There may be asymmetry of the chest with widening of the intercostal spaces. Percussion may elicit shifting tympany and dullness. Auscultation may show gurgling, tinkling, or a splashing sound in the chest region to the left or right or both sides.

Diagnosis.—The roentgenologist will be invaluable with most careful study and examination, without contrast medium, with barium, and by fluoroscopy, and may help in determining the method and course of treatment. Seidlitz powders will distend the stomach with gas and may be of material aid.

Treatment.—Treatment depends a great deal on the size of the hernia. For small and medium cases conservative treatment is indicated. For large hernias, if more than one-third of the stomach has herniated, and especially those containing colon, surgery is indicated. The danger of intestinal obstruction is ever present. Fixation of the stomach to the diaphragm or to the hernial sac causes much difficulty in treatment. Fortunately, such complications are rare. Early surgical repair is, therefore, indicated.

Many papers on the surgical treatment of hiatus hernias have been published. Harrington has been one of the main contributors. A brief summary of these papers is as follows:

A. Palliative surgical treatment.
   Temporary or permanent interruption of the left phrenic nerve is of help in many of the small or medium hiatus hernias. It may prevent spasm in small hernias.

B. Radical surgical repair of hiatus hernias.
   1. Temporary or permanent interruption of the phrenic nerve is indicated in many cases. Temporary crushing of the nerve will result in restoration of function in from three to six months. If the abdominal approach is planned it may be a wise preliminary step.
   2. Intratracheal anesthesia with use of positive pressure is essential.
   3. *Approach.*
      a. Abdominal approach. Harrington prefers the abdominal approach except in large hernias on the right side. He feels that the abdominal approach either through a subcostal or left rectus incision is preferable to the thoracic approach as the hernial contents are usually contained within a hernial sac in the posterior mediastinum. The hernial contents are not actually within the pleural cavity. The esophageal hiatus is to the left. He feels that there may be less complications than in a thoracic approach.
      b. Thoracic approach. Personally we agree with Sweet that the thoracic approach in the majority of cases makes the surgical technique somewhat easier. The hernial sac, the esophageal hiatus, the cardia of the stomach lie directly before one. The phrenic nerve can be crushed just above the entrance into the diaphragm at the beginning of the operation putting the diaphragm at rest. The freeing of the sac from the hernial aperture and the cardia of the stomach is simplified. The reduction of the hernial contents is easy. In very large hernias in which the reduction is more difficult Sweet has suggested making a separate counter incision in the diaphragm, reducing the hernial contents and temporarily drawing them through this counter incision over the lower edge of the chest wall wound until the hernial aperture has been closed. The objection of painful postoperative thoracic wounds has not been observed in sufficient numbers to be offered as a contraindication to the thoracic approach.
   4. In the abdominal approach the left lobe of the liver must be freed by cutting the suspensory ligament and either turning the lobe to the right, or bringing it forward into the wound, thus giving better access to the hiatus. The spleen must either be separated or, if necessary, removed.
   5. The sac of the hernia must be completely separated from the stomach. Its edges must be separated from the hiatus opening. The sac must be either totally removed or allowed to retract into the chest or mediastinum or plicated and dropped into the abdominal cavity as suggested by Sweet.
   6. Closure of the defect. It is well to pass a large stomach tube into the stomach at the time of closing the defect so that it will not be closed too tightly and cause difficulty in swallowing. One should be able to insert the tip of the index finger between the esophagus and the closed defect. The repair should preferably be either to the left

or behind the esophagus. Overlapping repair of the muscle edges should be accomplished with silk or cotton sutures. Interweaving of living fascia lata obtained during operation by an assistant is of great value in difficult cases as advised by Harrington. The esophagus may be incorporated in the suture. Great care must be exercised not to perforate the stomach if erosion or ulceration exists.

7. Exploration of the abdomen for other conditions is advisable if the abdominal approach has been employed. Immediate attention to abnormal findings, however, may not be advisable. Operations for secondary pathological findings should only be performed if absolutely essential.
8. Recurrence of esophageal hiatus hernias is not uncommon. Sweet has shown that recurrence seems to be much less frequent at the Massachusetts General Hospital following thoracic approach and repair than following the abdominal approach. If a recurrence should occur following repair by the abdominal approach the secondary operation should always be by the thoracic approach. If, therefore, recurrences are less frequent by the primary thoracic approach this method seems to be the method of choice.

CASE REPORT

CASE 1.—A young girl, E. L., 23 years of age was admitted to the Lenox Hill Hospital in November, 1947, with a complaint of nausea, vomiting, epigastric pain of three years' duration. These symptoms began three years previously and occurred in the evening at the end of a day's work. Vomiting gave relief. The attacks became more frequent until they occurred several days in a row. The attacks never occurred if the patient stayed in bed or was lying flat. Roentgenograms were taken three years previously and a diagnosis of hiatus hernia made at that time. The patient had lost fifteen pounds in the year previous to admission.

Gastric analysis showed free hydrochloric acid of 38 and total acidity of 46. The string test, after a white diet, showed a positive blood stain. There was a secondary anemia of 3,300,000 red blood cells, 9.6 Gm. hemoglobin or 64 per cent, 6,900 white blood cells with 66 per cent filaments and 9 per cent nonfilament polymorphonuclear leucocytes, 21 per cent lymphocytes, 2 per cent monocytes, and 2 per cent eosinophiles. The sedimentation rate of the blood was normal. The weight of the patient was 115 pounds.

X-ray Examination.—The liver was normal in size and its position was right-sided. The hepatic flexure of the colon was outlined by gas and was slightly low in position. X-ray examination of the chest showed the heart and aorta to be normal in size and contour. Irregular linear shadows were seen over the lower third of the right lung field, indicating the presence of stomach or intestine in the right thorax. The right leaf of the diaphragm could not be made out. The lungs were clear and well aerated throughout (Fig. 1).

Alimentary Tract.—Examination of the alimentary tract by means of a barium meal demonstrated that the entire stomach projected through a hiatus type of diaphragmatic hernia, the opening of which was probably not more than two inches in diameter. The entire stomach occupied the lower third of the right thorax posteriorly. The duodenal loop was in its normal position. At six hours only the traces of barium remained in the stomach. The remainder of the meal progressed at an average rate. The course of the small and large intestine was normal, the cecum being situated to the right, but the distal portion of the transverse colon was contained within the diaphragmatic hernia (Figs. 2 through 5).

Preoperative Preparation.—The patient was prepared with penicillin preoperatively, 30,000 units every three hours. Low residue diet was given. A Levine tube was passed and the stomach lavaged with soda bicarbonate and Wangensteen suction.

Operation.—On Nov. 25, 1947, the operation was performed using intratracheal anesthesia, gas, oxygen, ether, and cyclopropane.

In this instance on account of the extensive right-sided thoracic hernial contents it was decided to employ an abdominal approach. (Technical difficulties during the operation later proved this to be an unwise decision.) Therefore a left oblique per rectus incision was made

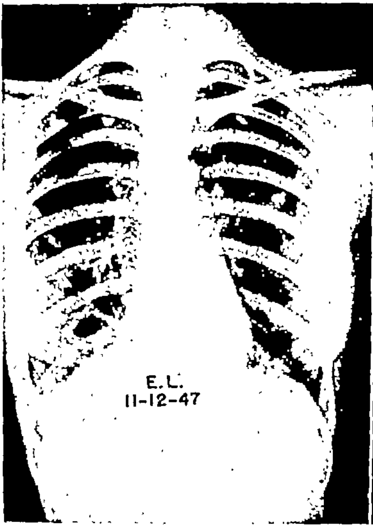

Fig. 1.

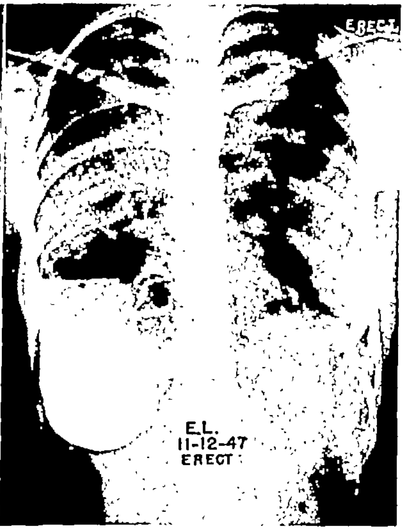

Fig. 2.

Fig. 1 (E. L.).—X-ray view of chest before barium meal. Esophageal hiatus hernia.
Fig. 2 (E. L.).—Barium meal showing stomach in right thoracic cavity. Erect posture.

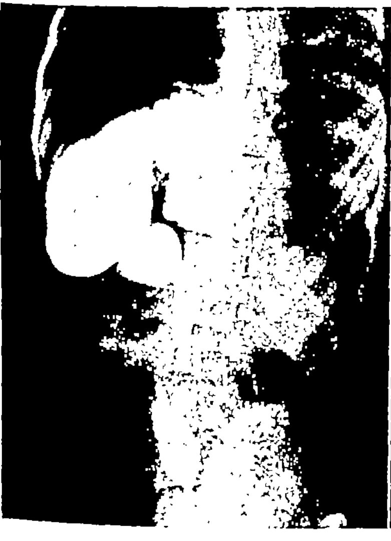

Fig. 3.

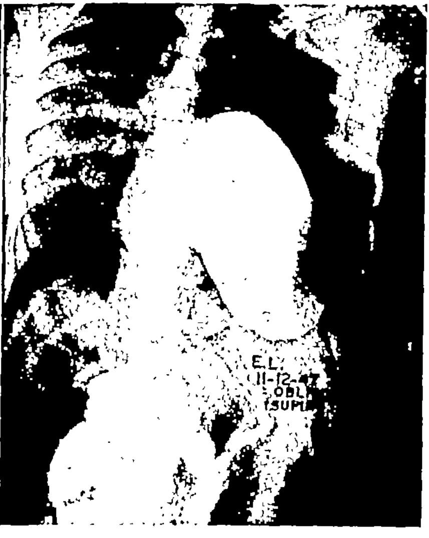

Fig. 4.

Fig. 3 (E. L.).—Oblique view.
Fig. 4 (E. L.).—Oblique supine view showing stomach high up in right thoracic

from the ensiform cartilage downward and outward to the level of the umbilicus. The abdominal cavity was entered. The stomach was not seen. The colon was seen passing into the right chest through the hiatus opening. The left lobe of the liver was freed by dividing the suspensory ligament and, thereby, exposing the hiatus opening. With a stick sponge in the hiatus opening air was sucked into the hernial sac making reduction of the hernial contents easier. The colon was withdrawn first and was followed by the entire stomach and omentum. The stomach had rotated 180 degrees so that the greater curvature was cephalad and the lesser curvature caudad. Step by step the hernial sac was separated from the cardia anteriorly, laterally, and posteriorly, exposing the esophagus. This procedure was more difficult especially on the posterior aspect of the stomach through the abdominal approach. Transthoracic access would have been much simpler. Hereupon, the parietal portion of the hernial sac was separated from the margin of the hiatus opening and the two widely separated crura of the diaphragm overlying the aorta. The peritoneum of the hernial sac was then allowed to recede upward into the right chest cavity. A large stomach tube was introduced into the stomach, and the hernial aperture then repaired. The hiatus opening was closed around the esophagus employing silk mattress sutures—three ventral to the esophagus, and two dorsal to the esophagus. Here the tissues were poor in quality. After tying of the sutures, it was felt that the esophageal opening was too tight. Therefore, one ventral silk suture was removed and replaced with a cotton suture. Cotton sutures were then employed to reinforce the silk mattress sutures. The left lobe of the liver and the spleen fell into place and came up to the repaired hiatus opening. The stomach and colon were then placed in the proper position. The stomach was found to be unusually large and filled a large portion of the left part of the abdominal cavity. The abdominal wall was closed in layers employing interrupted silk sutures.

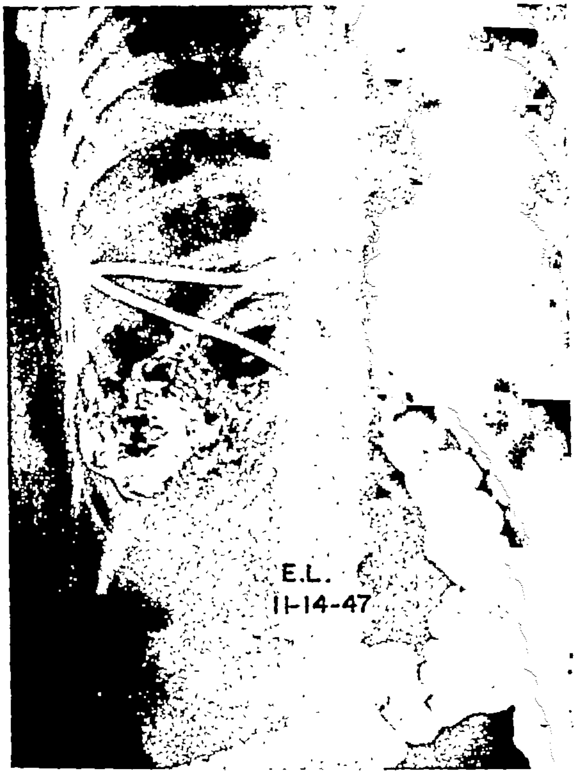

Fig. 5 (E. L.).—Forty-eight hour view. Barium in transverse colon within right thoracic cavity. Note Levine tube in stomach.

The patient received 500 c.c. of blood and 1,500 c.c. of saline with glucose during the operation. She left the operating room in good condition.

Postoperative Course.—The patient made an uneventful surgical convalescence. However, a gastrointestinal x-ray examination on the thirteenth postoperative day showed a very large atonic stomach within the abdomen. There was marked 24- and 48-hour gastric retention (Figs. 6 and 7). The barium immediately passed through the pylorus at the time of examination and filled the duodenum. There was practically no evidence of peristaltic activity in the stomach. At 6 hours practically 75 per cent of the barium was retained in the stomach. The remainder of the meal was progressing normally. At 24 hours and 48 hours there was at least 50 per cent retention in the stomach. A gastric analysis showed a total absence of free hydrochloric acid with a total acidity of only thirty. Fractional gastric analysis with histamine performed on December 16 showed a total absence of free hydrochloric acid over the 90-minute period. The total acid went up to 40 at the end of one hour and dropped to 20 at 90 minutes. A Hollander insulin test showed an absence of free hydrochloric acid with a total acidity of 16 with the blood sugar dropping to 22 mg. per cent at 30 minutes and rising again to 83 mg. per cent at 2 hours. The possibility of injury to both vagus nerves at the time of separation of the peritoneum from the cardia of the stomach was considered.

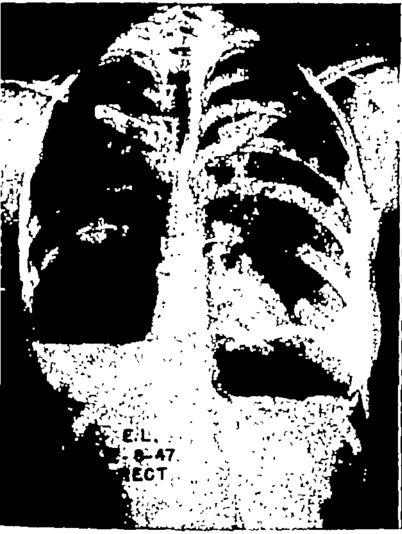

Fig. 6.

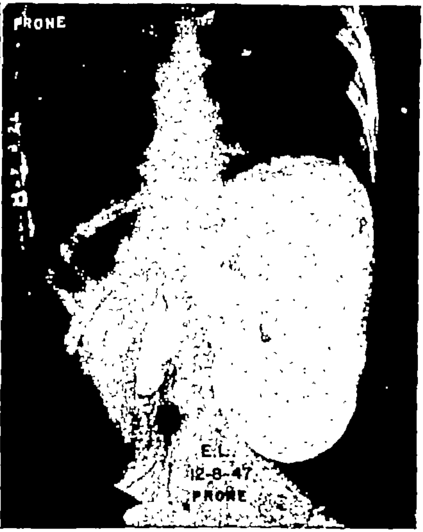

Fig. 7.

Fig. 6 (E. L.).—X-ray view of chest postoperative showing fluid level in empty hernial sac within right thoracic cavity. Note barium passing normally into stomach within abdominal cavity.

Fig. 7 (E. L.).—Showing large atonic stomach filling left side of abdominal cavity.

The patient was discharged from the hospital on December 20. Early in January she was put on Urecholine as a trial to see whether the atony of the stomach would improve. At the end of January x-ray studies were repeated (Fig. 8), and there was still evidence of gastric atony but to a lesser degree. There was still 24-, 48-, and 72-hour retention. The

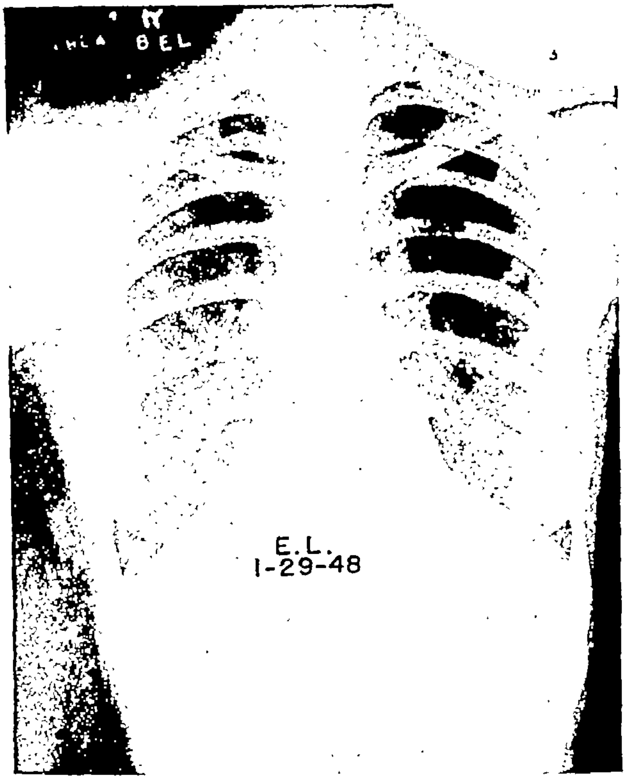

Fig. 8 (E. L.).—X-ray view of chest two months after operation showing complete absorption of fluid from hernial sac in right thoracic cavity.

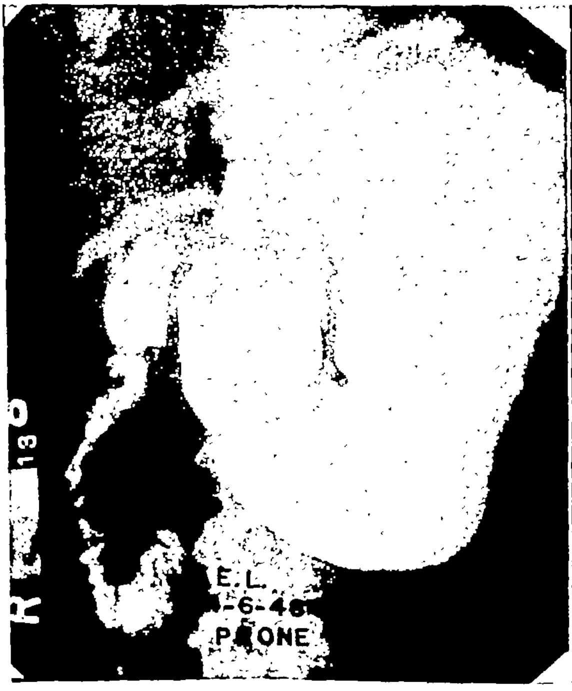

Fig. 9.

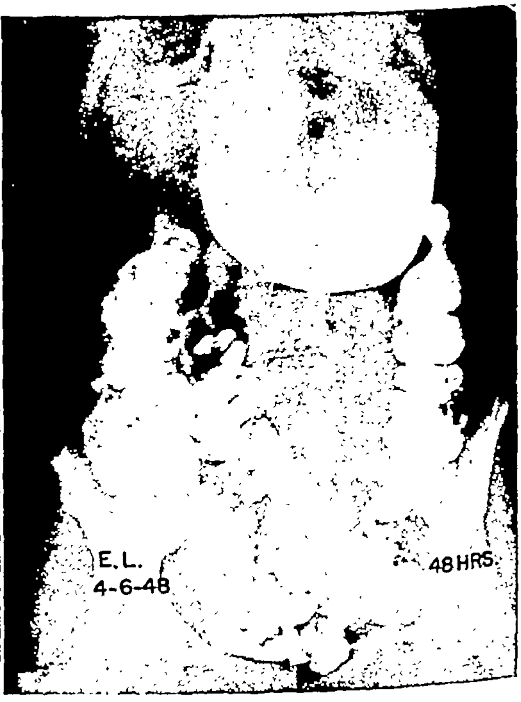

Fig. 10.

Fig. 9 (E. L.).—Showing large atonic stomach 4 months after operation.
Fig. 10 (E. L.).—Showing 48 hour residue in stomach 4 months after operation.

stomach was well within the abdominal cavity, but a very small pouch of the stomach protruded upward through the esophageal hiatus. The peritoneal sac in the right chest did not show the fluid level and air within the sac which had been seen postoperatively. The patient was doing well, but gastric lavage was necessary to keep her comfortable in an attempt to improve the condition of the gastric musculature.

The patient was readmitted to the hospital for study in April and June, 1948 (Figs. 9 and 10). Each time there was evidence of increasing free hydrochloric acid on gastric analysis with histamine, and the total acidity had also increased. The Hollander insulin test showed the usual drop in blood sugar but not a concomitant rise in free hydrochloric acid. X-ray examination showed the size of the stomach to be smaller, but there was still marked atony with very little evidence of peristalsis. It is interesting to note in this case that the patient to a degree had adjusted herself to the presence of the stomach within the right chest cavity. After replacement of the stomach into its normal position within the abdominal cavity, it was found that the stomach did not function as normally as one had hoped it would. In July, 1948, the patient was feeling very well, gaining weight, and worked a full day. Only occasionally did she lavage her stomach.

In retrospect a thoracic approach would have been preferable in the repair of this hernia. Access to the enlarged esophageal hiatus would have been easier. Separation of the peritoneal hernial sac from the cardia of the stomach especially posteriorly and from the margins of the hernial aperture would have been much easier. Crushing of the phrenic nerve intrathoracically would have been advantageous. The apparent injury to vagus nerve fibers with marked postoperative gastric atony might have been avoided. The convalescence would have been markedly simplified thereby.

CONGENITAL HERNIA

Historical.—Ladd and Gross, Harrington, Truesdale, Donovan, Dorsey, and Marks have written extensively about congenital hernias. Orr and Neff, in 1936, found only 17 patients operated in the first year of life. Of these only 9 survived. There is little to recommend delay.

Types.—1. The commonest hernia occurs through the pleuroperitoneal hiatus or the foramen of Bochdalek. 2. They may also occur through the esophageal hiatus. That the latter is the commonest type in adult life is due to the fact that babies with congenital hernias through the foramen of Bochdalek have had such a high mortality. 3. The third type are the congenital hernias through the foramen of Morgagni or the substernal hernias. These hernias are more common on the right side.

The hernias through the foramen of Bochdalek have no hernial sac while those through the foramen of Morgagni have a hernial sac.

Symptoms.—The symptoms are severe. Death is frequently caused by asphyxia or intestinal obstruction. Respiratory, circulatory, or gastrointestinal, or a combination of these three main symptoms may be present. If there is dyspnea, cyanosis, or vomiting during crying or nursing following delivery, immediately suspect a congenital diaphragmatic hernia.

Physical Signs.—

1. Rapid respiration and pulse rate.
2. Heart displaced from the affected side.
3. Tympany or dullness on percussion of the affected side.
4. Absent or distant breath sounds on auscultation, also the presence of intestinal gurgles.

5. Scaphoid abdomen as most of the abdominal contents are in the chest, especially the small and large intestines, usually with nonrotation of the colon. The spleen, omentum, and possibly portions of the liver may be in the chest.

Diagnosis.—The suspicion of the presence of diaphragmatic hernia is the main diagnostic feature. X-ray evidence is of value, preferably without contrast medium.

Treatment.—It is the consensus of those authors who have had greatest experience such as Ladd and Gross, Donovan, and Harrington that the earlier the repair is performed the better the chance of survival of the infant. The abdomen does not develop properly without its proper contents, if the hernial contents are permitted to remain in the chest. While some few infants may accommodate themselves to the presence of the abdominal contents in the chest, their later return to the nondeveloped abdomen becomes almost an impossibility. Therefore, the safest and wisest procedure is surgery as quickly as the diagnosis is made. Newborn infants stand major surgical procedures better than they do a week or more after birth. The youngest infant operated by Ladd and Gross was only forty hours old. The first forty-eight hours are the best, the intestines are not as distended and can be returned more easily into the abdominal cavity.

Preoperative Preparation.—

1. Hydration.
2. Enemas to deflate the bowel.
3. Gastric suction.
4. Oxygen tent with 95 per cent oxygen.

Anesthesia.—Cyclopropane with positive pressure by intratracheal tube.

Operation.—

1. Preliminary phrenic crush in the neck.
2. Almost invariably the abdominal approach for the repair of the hernia.
3. Incision—vertical or subcostal.
4. Allow air to enter the chest through a catheter and then contents can be more easily withdrawn.
5. Denude the edge of the hernia ring of the serous membrane.
6. Suture the opening in the diaphragm with two rows of silk or cotton mattress sutures.
7. Insert a catheter into the chest before closing the last suture so that the air can be sucked out of the chest in order to expand the collapsed lung before tying the last suture.
8. The physiology of respiration is affected by the repair of the diaphragmatic hernia. The sound lung is compressed by increased intra-abdominal pressure on returning the intestinal contents to the abdomen before the bad lung has had a chance to expand fully.

Therefore, if any difficulty is encountered on returning the intestinal contents into the abdominal cavity, Ladd and Gross have proposed a two-stage operation. They believe that their mortality has been greatly reduced by this procedure. They cut the rectus muscle transversely after under-cutting the skin in order to be able to slide the abdominal wall across the intestinal contents by only suturing the subcutaneous fascia with interrupted mattress sutures and then closing the skin. After the abdominal wall has stretched sufficiently, the incisional hernia is repaired. This is done about five or six days after the first operation. Dorsey stretched the abdominal wall manually and used drop ether anesthesia for deeper relaxation. Ladd and Gross feel that the two-stage operation is preferable to a difficult one-stage closure for the following reasons:

1. It is less shocking.
2. It avoids strain on the suture line of the diaphragm.
3. It avoids postoperative embarrassment of respiratory and circulatory systems.

Harrington advises an x-ray examination in the operating room at the termination of the operation to make sure that the mediastinum is in the center after the air has been withdrawn through the catheter during the operation. If the mediastinum is not in the center, more air must be withdrawn from the chest before returning the infant to the ward.

Postoperative Care.—

1. Oxygen tent relieves respiration and abdominal distention.
2. Fluid requirements parenterally with small transfusions in order not to embarrass the right heart.
3. Fluids by mouth.
4. Watch for pleural effusion.

CONGENITAL ABSENCE OF THE DIAPHRAGM

This is a rare condition. Sagal, in 1933, collected only twelve cases. Dr. William J. Mayo operated on Beckman's case and proved its presence by operation. The positive diagnosis can be made only by operation and determination of the condition by a competent surgeon.

The defect extends from the eighth rib in the posterolateral portion of the diaphragm and extends medially to the esophageal hiatus. There is usually no sac. The opening is so large that the stomach, spleen, large and small intestines have passed through the aperture into the chest.

Treatment of these conditions is more difficult than hernias through the foramen of Bochdalek. It requires great surgical technical skill to bring the diaphragm to the chest wall or the chest wall to the diaphragm. The use of the perirenal fascia or the latissimus dorsi muscles (Rives and Baker) in the repair of the posterior defects is of value. Thoracoplasty with resection of one or more of the lower ribs is occasionally also required. Permanent interruption of the phrenic nerve is necessary.

CONGENITAL SUBCOSTAL-STERNAL HERNIA THROUGH FORAMEN OF MORGAGNI

This is a direct hernia through a congenital defect by failure of fusion of the sternal and costal portion of the anterior diaphragm.

There is always a sac as in an esophageal hiatus hernia. It is the rarest type of hernia while the esophageal hiatus hernia is the most frequent.

The contents are usually colon, omentum, or intestine, rarely the stomach. These pass through a congenital weakened defect later in life due to increased intra-abdominal pressure.

The symptoms are pain, cough, dyspnea, and occasionally intestinal obstruction. The physical findings and x-ray films may make one suspicious of a primary pulmonary lesion, especially if only omentum is in the hernial sac. The lesion being anterior, lateral x-ray films will help one to determine the possibility of this type of hernia if the pathology is close to the diaphragm and anterior.

Treatment of this type of lesion is by surgery. Abdominal approach is by far the best. An oblique rectus incision is advantageous. The round ligament of the liver can be incorporated in the repair if the hernia is on the right side. If the opening is large, the phrenic nerve should be interrupted. The transversus abdominis muscle, which is normally continuous with the diaphragm muscle, may be employed in the repair of the defect.

CONGENITAL SHORT ESOPHAGUS WITH PARTIAL THORACIC STOMACH

The repair of this condition has been reported by Harrington. Permanent interruption of the phrenic nerve is necessary in order to be able to close the diaphragm above the cardia and around the esophagus. By freeing the esophagus thoroughly, the esophagus can be brought down some centimeters.

EVENTRATION OF THE DIAPHRAGM

This is a rare condition more common in men than in women. It is more common on the left side than on the right side, but may be bilateral especially in cases of megacolon. The condition may be acquired or congenital and is caused by aplasia or atrophy of the muscle fibers of the diaphragm.

In 1921, Korns published a comprehensive analysis of proved cases.

The diagnosis is made by the roentgenologist. The differential diagnosis is between a hernia with a sac or eventration of the diaphragm. An arched line above the organs may be either.

The diaphragm may be demonstrated by a pneumoperitoneum. The loops of bowel are drawn together more in a hernia than in an eventration. Symptoms are much less severe in eventration than in a hernia. There is frequently a feeling of pressure in the left chest caused by gas in the stomach above the level of the cardiac orifice. The heart is usually found on the right-hand side. Symptoms like this frequently occur after phrenic crushing in tuberculosis.

TRAUMATIC DIAPHRAGMATIC HERNIA

These are always false hernias without sacs as the diaphragm is torn by penetrating injuries, crushing injuries, or falling injuries. In World War II there were many injuries of the diaphragm caused by shell fragments, bullets, or other missiles. They may occur anywhere in the diaphragm, but the very great majority are on the left side. The diaphragm is frequently torn from the dome all the way to the periphery. It is comparable to an evisceration of the abdominal contents into the pleural cavity. The stomach and large and small intestines may have herniated through the opening, and signs of intestinal obstruction may be among the first symptoms. The symptoms are severe and progress rapidly. There is interference with the function of the lungs and heart. Adhesions develop along the margins of the hernial orifice.

Treatment is always by surgery. The best approach in this case is transthoracic as it gives better access and makes separation of adhesions easy. The diaphragm can be paralyzed by intrathoracic crush of the phrenic nerve. The margins of the hernial aperture must be debrided and then repaired by careful overlapping suture. Cotton or silk may be used, but living fascia lata is of value if the operation is one of election in a hernia present some months after injury or following inflammatory or pressure necrosis. The diaphragm may be sutured to the intercostal muscle, preferably to two intercostal spaces, if the tear goes all the way to the periphery. Lower thoracoplasty of the eighth, ninth, and tenth ribs should be kept in mind if this is indicated in the proper closure and repair of the diaphragm.

Negative pressure must be re-established by withdrawing air through a catheter, and air-tight underwater drainage is wise especially if contamination of the pleura has taken place. Antibiotics and chemotherapy also are of great value. Aspiration of air from a pneumothorax is important until negative pressure exists.

The replacement of the abdominal organs from the pleural cavity must be orderly. If obstruction exists, an appendicostomy or colostomy may wisely be added. Wangensteen suction of the stomach is required.

Intratracheal anesthesia with positive pressure is essential.

Postoperative oxygen is necessary.

CASE REPORTS

Case reports of three traumatic diaphragmatic hernias are appended:

CASE 1.—A sergeant was admitted to an evacuation hospital two and one-quarter hours after having been hit by a shell fragment. The wound of entrance was in the left posterior axillary line over the tenth rib. It measured about 4 cms. in length. Omentum presented itself in the wound of entrance, having prolapsed through the diaphragm and pleural cavity into the wound of entrance. X-ray examination showed a shell fragment in the region of the left lobe of the liver.

After proper preoperative therapy, the soldier was operated upon under intratracheal anesthesia. The superficial wound was debrided and the ninth rib resected. The pleural cavity was filled with blood, and the lower lobe of the left lung was lacerated. It was repaired by suture after debridement.

The diaphragm was badly torn, and a torn, bleeding spleen had herniated through the hole in the diaphragm. The eighth rib was then resected for better access. The diaphragm was debrided and then incised medially and laterally for better access to the abdominal cavity. The spleen was removed. A 4-cm. rent in the posterior wall of the stomach was closed near the greater curvature. The wound of exit on the anterior wall of the stomach near the lesser curvature was then closed. The shell fragment could be palpated just under the surface of the dome of the left lobe of the liver near the midline. The foreign body was removed from the liver, and the cavity in the liver was drained bringing the drain out through a stab incision made in the anterior abdominal wall. No further damage could be found within the abdomen.

The diaphragm was then repaired with interrupted overlapping sutures of the leaves with silk sutures. The left phrenic nerve had been crushed. The pleural cavity was irrigated with saline, and 40,000 units of penicillin were instilled. Air-tight underwater drainage was instituted. The chest wall was closed and air withdrawn; 3,000 c.c. of blood in Alsever's solution were given during the operation. A Levine tube had been introduced into the stomach on admission and was left in place with Wangensteen suction.

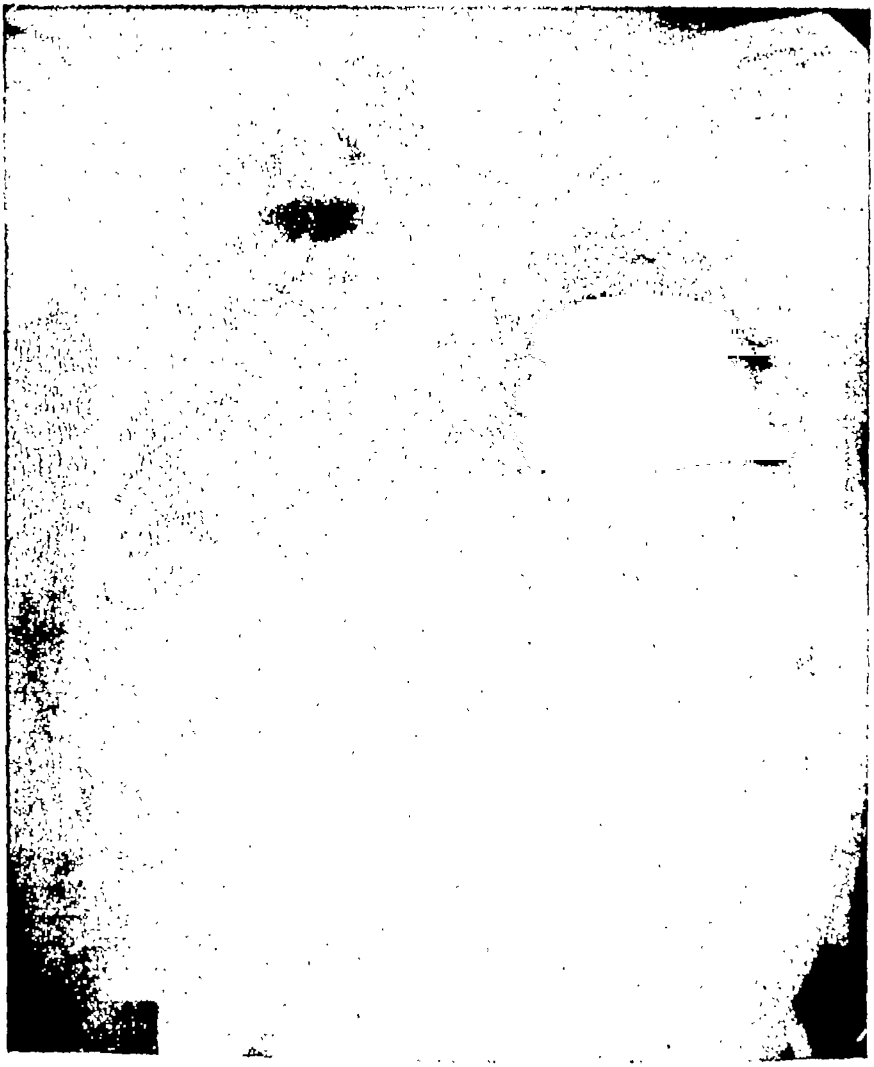

FIG. 11 (J. C., Case 2).—Traumatic diaphragmatic hernia. Note tremendously dilated stomach filled with fluid in left pleural cavity. Heart and mediastinum shifted to right. Patient admitted to hospital in shock.

The patient did well and the pleural drain was removed in 48 hours and the skin wound closed with sutures. Penicillin and sulfadiazine were continued after the operation.

The anterior abdominal drain was changed on the tenth day postoperatively. Fluid was aspirated once from the left pleural cavity. The patient was evacuated on the twenty-second postoperative day. He finally reached England where he was seen by Col. Harken. All wounds were healed six weeks postoperatively.

Three months after his injury he was returned to general duty. While the patient was waiting in the replacement depot the chest wound reopened. He was then operated on for empyema and returned to the United States. At Camp Shanks an abscess of the abdominal drainage wound was opened. While in the Brooke General Hospital, both wounds healed. While the patient was home on furlough in Rochester, Minn., the chest wound reopened. Later, at operation at Brooke General Hospital, two silk sutures used at the original operation for repair of the diaphragm were found in the abscess cavity. Hereupon, the wound healed and has remained healed. *The traumatic diaphragmatic hernia has also remained healed.*

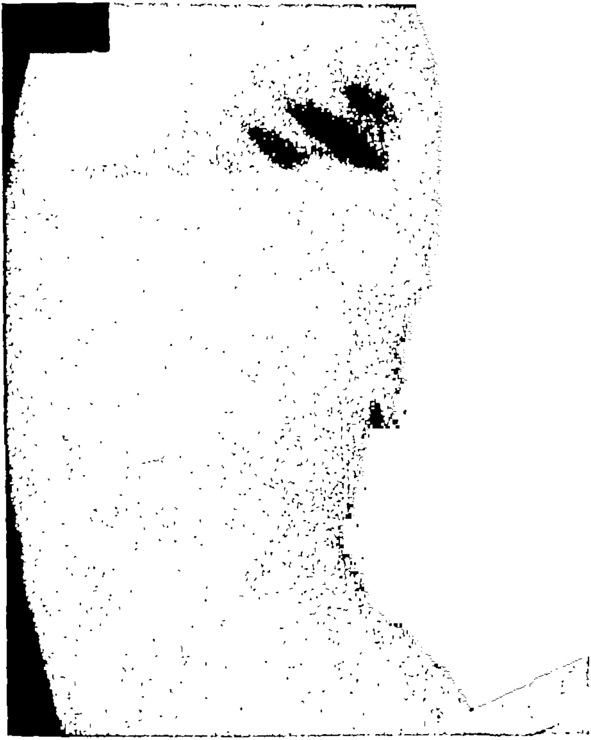

Fig. 12 (J. C.).—Lateral view of chest showing similar findings.

Case 2.—A soldier, private, 10 years of age, was admitted with a diagnosis of perforating gun-shot wound of the left chest wall and diaphragmatic hernia. The wound of entrance on the anterior left lower chest and the wound of exit in the posterior axillary line lower down had been debrided at a more forward installation and had been covered with petroleum jelly gauze. The soldier was admitted in shock, which had developed in transport. Pulse was 150, heart shifted to the right, there were absent breath sounds in the left chest. X-ray examination showed a huge fluid level in the left chest (Figs. 11 and 12). The patient had been evacuated by ambulance without a Levine tube in place and with a diagnosis of herniation of stomach through the left diaphragm. On introducing a Levine tube with suction 1,200 c.c. of dark fluid and much gas was obtained. The heart shifted back to the midline, respirations and pulse rate decreased. X-ray examination showed a marked decrease in the size of the stomach and the heart again in normal position (Fig. 13). Chemotherapy was started and the patient prepared for operation. He was operated upon under intratracheal anesthesia. The fractured eighth rib was widely resected. The omentum was found adherent in the wound of entrance in the chest wall. The pleural cavity was then entered.

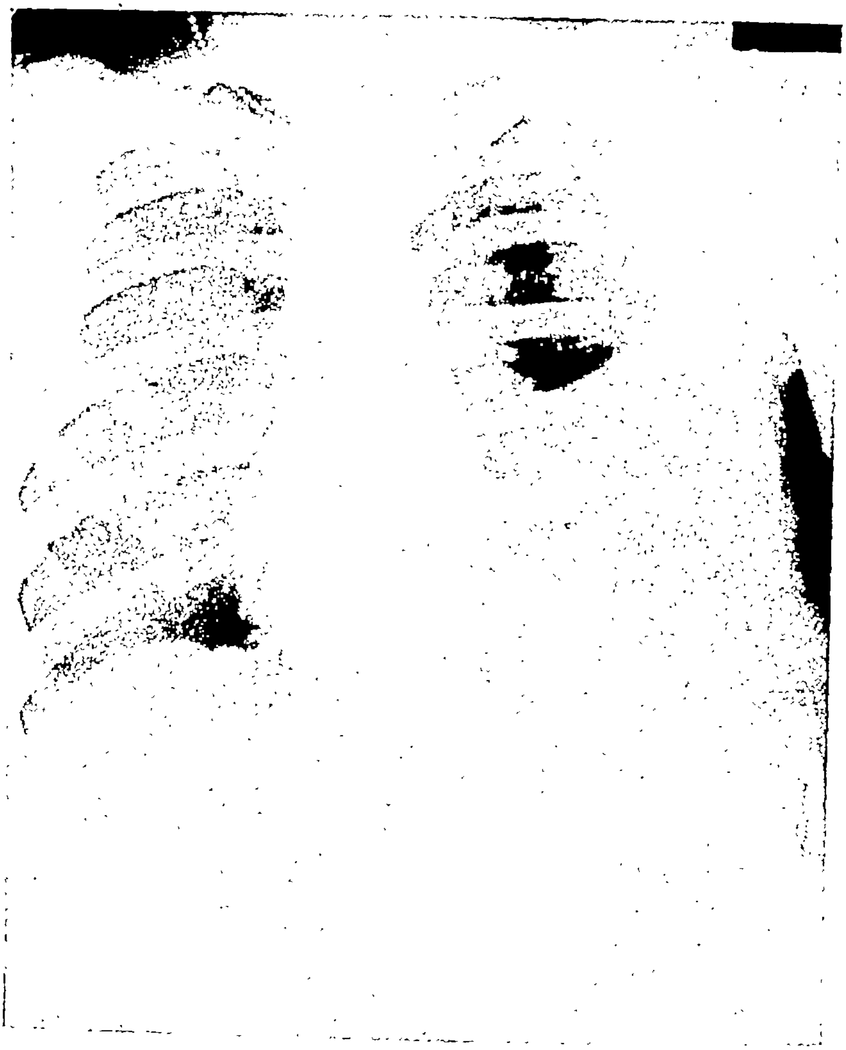

Fig. 13 (J. C.).—Levine tube passed. Stomach emptied. Heart and mediastinum have shifted back to midline. Patient immediately recovered from shock condition and prepared for operation.

The entire stomach and a portion of the transverse colon and omentum were in the left pleural cavity and had twisted 180 degrees through the longitudinal axis of the stomach. The organs were adherent to the torn edges of the diaphragm. They were separated. The diaphragm was incised for about 6 cm. to permit proper reduction of the hernial contents into the peritoneal cavity with exploration. The phrenic nerve was crushed. The wound of the diaphragm was debrided. The hernial aperture was repaired by interrupted mattress sutures of silk reinforced by fine sutures of silk. The chest was closed with air-tight underwater drainage and the air sucked out of the pleural cavity. The patient had to be evacuated to a holding company and was later evacuated to the zone of the interior.

The patient now lives in Philadelphia and through the courtesy of Dr. Gilson Engel and Dr. Farrell, this patient has been examined by fluoroscopy in December, 1947. Everything has been found normal with the diaphragm well healed.

CASE 3.—A sergeant was admitted in shock following a jeep accident. The right chest was crushed and there was a fracture of the right femur. He was treated for shock with blood and plasma. On admission his blood pressure was 60/40 with pulse 136. Penicillin and sulfonamide therapy were started. When the patient's condition was satisfactory, he was operated upon under intratracheal anesthesia. A transverse incision was made from the costosternal junction on the right side to the posterior axillary line over the sixth, seventh, and eighth ribs. These ribs were severely comminuted and the parietal pleura badly torn. The pleural cavity was filled with about 600 c.c. of bright red blood mixed with fragments of liver tissue. The lung was contused but intact. There were two lacerations of the diaphragm, probably caused by the rough comminuted rib ends. These two lacerations were joined exposing a large wound of the dome of the right lobe of the liver which was bleeding and many loose fragments of liver tissue were in this hole and in the pleural cavity. A subcostal incision was then made through the abdomen, and two gauze packs and a Penrose drain were placed into the large hole in the liver measuring about 10 cm. in diameter. These were brought out through the abdominal incision. The diaphragm was then sutured with interrupted silk mattress sutures reinforced with chromic sutures. The pleural cavity was then irrigated with saline and the chest wall closed in layers. The pleura could not be sutured as it was too badly torn. The lung was inflated, air sucked out of the pleural cavity, and air-tight underwater drainage instituted in the eighth interspace posteriorly.

The fractured femur was in a Thomas splint and temporarily left in it. The pleural drain was removed on the third postoperative day and a cast applied to the fractured femur. On the seventh day the liver tampons were removed and the Penrose drain left in situ. The chest wound was healed by primary union. The patient was evacuated to the zone of the interior.

Since that time, we have been able to communicate with this patient in February, 1948, and found out that the Penrose drain was removed at a rear installation immediately upon arrival. He then developed a subphrenic abscess which perforated through the torn diaphragm into the pleural cavity giving him an empyema. This was drained and healed without further complication, and he is at present perfectly well.

COMMENT

1. An understanding of the normal anatomy and the embryologic development of the diaphragm is necessary to properly evaluate the surgical problems presented.

2. Harrington and Marks have both given us excellent workable classifications of diaphragmatic hernias.

3. Certain types of hernias are amenable to surgical repair while others cannot be repaired.

4. The true short esophagus with thoracic stomach cannot be treated surgically. It is a rare anomaly. All or nearly all of the stomach is in the mediastinum.

5. Diaphragmatic hernia with shortened esophagus may be treated surgically by permanent phrenic section, freeing of the esophagus for lengthening, and closing the diaphragm above the cardia. Constriction at the junction of the esophagus with the stomach may cause dysphagia in these cases.

6. Hiatus hernias are the most common type. The esophagus is not short. It can be repaired surgically if the symptoms warrant it. The thoracic approach is probably the best and most practical, although this may be a matter of choice with the individual surgeon.

7. Congenital hernias occur most commonly through the foramen of Bochdalek, through the absence of a portion of the diaphragm; least frequently through the foramen of Morgagni, which hernias usually develop later in life. The earlier in life congenital hernias are operated upon the better. There is no benefit in delay. Two-stage closure of the abdomen in some instances will lower the mortality. The abdominal approach is by far the best. Circulatory, respiratory, and gastrointestinal symptoms are severe and may cause death by suffocation and cardiovascular collapse. In hernias through the foramen of Morgagni the abdominal approach should also be employed.

8. Eventration of the diaphragm is an infrequent condition. Symptoms are less marked than in hernias. The main differential diagnosis is between it and a true congenital hernia. Surgery is not indicated.

9. Congenital absence of the diaphragm is rare. It must be proved by surgical exploration but must previously be considered in the differential diagnosis.

10. Traumatic hernias are accompanied by severe symptoms, often with signs of intestinal obstruction. They interfere with the circulatory and respiratory symptoms. Surgery is indicated. The transthoracic approach is best.

CONCLUSIONS

1. Diaphragmatic hernia is diagnosed much more frequently now than formerly.

2. It must always be considered in the differential diagnosis of upper abdominal pathology.

3. Surgery will repair many of these hernias successfully.

4. Intratracheal anesthesia with positive pressure should be available.

5. Proper preoperative preparation, meticulous operative technique, and careful postoperative care will lower the former high mortality.

6. All types of diaphragmatic hernias are discussed and their treatment of choice enumerated.

7. Several case reports are included.

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LIPOID PNEUMONIA RESULTING FROM A DERMOID CYST

Case Report

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THE case presented herewith is deemed worthy of reporting because of the unusual source of the lipoid material which produced the lipoid pneumonia.

Lipoid pneumonia is customarily considered to have its origin from the inadvertent entrance of lipoid material into the tracheobronchial tree.

Animal and mineral oils are known to cause tissue reactions, whereas neutral vegetable oils have been shown to be practically innocuous.[1, 2, 3]

The diagnosis of lipoid pneumonia in the case herewith presented was first established by a biopsy taken November, 1945, two years before the patient's present entry, when a mediastinal lymph node showed scarring and high fat content. It was again confirmed by us bronchoscopically, at the present entry. Operation revealed the unexpected finding of a large dermoid cyst, the cavity of which contained viscid animal oil. This cavity communicated directly into the primary bronchus of the left upper lobe. The lipoid substance was thus disseminated directly into the left upper lobe and by spill-over to a lesser extent, into the lower lobe. This source accounted for the unilateral and diffuse character of the lesion which involved all of the left lung but with maximum disease in the upper lobe into which the dermoid directly drained. The history of the use of oily nose drops for many years by this patient suggested preoperatively this to be the source of her lipoid pneumonia. However, histochemical studies* of the oil in the lung after its extirpation have shown the offending oil to be the unsaturated type, thus excluding mineral oils. Therefore, we must conclude that the oil which caused the lipoid pneumonia was derived from the patient herself (i.e., the dermoid) and that the oily nose drops were merely incidental and had no bearing on the production of the lipoid pathology.

CASE REPORT

History (Essential).—The patient (D. P.) a 20-year-old white woman, well developed and fairly well nourished was first seen at the Mount Zion Hospital on July 28, 1944. Complaints then consisted of repeated attacks of cough, fever, and expectoration for as long as she could remember. She had used oily nose drops frequently and regularly since childhood. At this time there were also painful swellings of the joints, especially of the fingers and left wrist. These were suggestive of rheumatoid arthritis. Routine blood and urine studies were negative except for an elevated sedimentation rate. X-ray examination of the chest showed a 10 by 5 cm. hilar mass extending towards the left, suggestive of tuberculosis or lymphoma. A therapeutic trail of x-ray radiation was given with no resolution of the hilar mass.

During the subsequent fourteen months she was readmitted to the hospital three times with the same complaints. Bronchoscopy then revealed what was considered to be a mild

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From the Thoracic Surgery Division of the Department of Surgery of the Mount Zion Hospital.

Read (by title) at the Twenty-eighth Annual Meeting of The American Association for Thoracic Surgery, Quebec, Canada, May 31, June 1, 2, 1948.

*The histochemical analyses were made in the Department of Pathology of Mount Zion Hospital, by Dr. Gerson R. Biskind, Chief of the Department.

tracheobronchitis. Bronchograms showed the anterior and middle bronchi of the left upper lobe to be spread apart, apparently by extrinsic pressure resulting from a mass in the anterior mediastinum.

The mediastinal mass continued to enlarge and operative intervention was undertaken* in October, 1945. A dense mass of mediastinal nodes was encountered which, in spite of their previous failure to respond to radiation therapy, was considered to be lymphomatous in nature. Specimens were removed for histologic study and the wound was closed. Microscopic examination of these removed specimens was reported as showing hyperplasia of the regional lymph nodes with marked deposition of lipoid material in the sinusoids. The diagnosis was then considered to be lipoid pneumonia with regional lymph node involvement, the causative factor being attributed to the persistent use of oily nose drops.

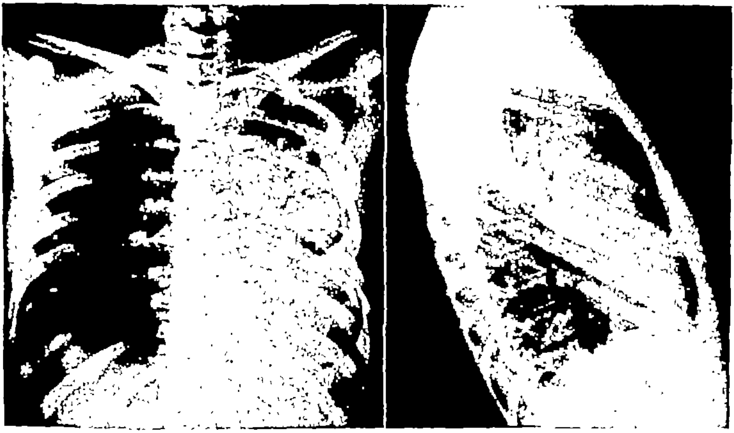

Fig. 1.—X-ray examination anteroposterior and lateral views. Shift of trachea and mediastinum to the left; entire left chest full of areas of varying degrees of increased density with peculiar rounded shadows of increased density currently surrounded by air in the mid-peripheral portion; thickened pleura; regenerated fifth rib.

Cessation in the use of the oily nose drops did not improve matters. Cough and bouts of fever increased in frequency, the sputum became very copious and finally foul; there ensued mild and severe hemoptyses. The mediastinal mass grew and both lobes of the left lung became involved in a chronic pneumonic process, most marked in the left upper lobe. Laboratory studies except for the continued elevated sedimentation rate remained essentially normal. These included negative tuberculin up to 1:100 and sputum studies for tumor cells.

The patient was first seen by me late in 1947, when, in view of the preceding course and findings, it was decided that nothing short of extirpation of the involved tissues might be of benefit. The lesion was considered to be a diffuse lipoid pneumonia, with marked bronchiectatic changes and extensive mediastinal lymph node involvement.

OPERATION

Dec. 30, 1947, *preoperative diagnosis:* paraffinoma left lung. Operation: left pneumonectomy. Anesthesia: intratracheal.

Procedure.—The chest cavity was opened through the fifth intercostal space. There was no free pleural space. The lung was adherent to the chest wall on all sides and moderately so to the pericardium. With blunt and sharp dissection the lung was freed from the chest wall. The large adhesions were clamped and tied. The upper and lower lobes of the lung had the consistency of liver tissue. They did not collapse nor did they fully expand. The upper lobe was a little more involved than the lower lobe but both were definitely fibrotic. The left leaf of the diaphragm did not move too well on respiration. The lateral half did not seem to move at all.

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*By Dr. Clayton Lyons.

Lying in the anterior mediastinum just under the sternum and in close relation to the root of the lung was a mass about the size of a turkey egg which at first was thought to be a lymph gland but when it was accidentally opened, it was found to be a dermoid cyst containing hair and an oily cheeselike material. After fine dissection the pulmonary artery was isolated and divided between ligatures. The inferior pulmonary vein was isolated; it coursed for a distance of 2 cm. and then divided into two main branches. The vein was then cut between ligatures. A similar procedure was carried out on the superior left pulmonary vein. The left main bronchus was then isolated and two ligatures of heavy white braided silk ties were placed and the bronchus was cut through. The lung was then removed and the bronchial stump was closed with 1-No. 1 silk interrupted sutures. The chest cavity was filled with normal saline and no air was seen to bubble through so that the bronchial stump was completely closed. All of the saline was aspirated by suction. No gross bleeding was evident. The closure of the chest cavity was undertaken. Sterile dry dressings were applied and the patient was turned on her back and bronchoscopy was done. The main bronchus to the right lung was found to be clear and there was considerable mucus in the posterior nasal pharynx which was aspirated and the patient was returned to the ward. During the procedure the patient received about two and one-half units of whole blood with the completion of the third taking place on the ward.

Postoperative diagnosis: (1) dermoid cyst anterior mediastinum; (2) paraffinoma left lung.

PATHOLOGY

Gross Description.—The specimen consisted of a left lung, a rounded mass of yellow-white tissue, and several smaller rounded masses of tissue said to represent hilar lymph nodes. The lymph node masses varied in size up to 3 cm. in diameter. They were firm and on section had a cream-yellow parenchyma which was mottled by red-brown zones. Several smaller similar lymph nodes were attached to the hilar portion of the lung. The lung possessed two lobes. The line of resection was 1 cm. proximal to the first division of the left main bronchus. The lung was 16 cm. from apex to base, 11 cm. wide, and 5 cm. in thickness. The pleura was red-brown in color and roughened by numerous thin tags of fibrous tissue. Near the center of the left upper lobe there was a space which was irregularly rounded and slightly collapsed. It had a diameter of 5 cm. This cavity lay 2.5 cm. from the interlobar septum. It was covered by 0.7 cm. of lung tissue on its medial aspect. The inner surface of this cavity was shaggy with a gray-brown color. It contained yellow cheesy material and numerous blond hairs. A communication from this cavity into a large branch of the upper lobe bronchus was identified. The rounded yellow-cream-colored mass mentioned previously was said to have occupied the cavity within the lung parenchyma and to have been freed from this space during surgery. This mass measured 7 cm. in greatest length and 5 cm. in greatest width. It was irregularly rounded. Its surface had the appearance of skin and bore numerous blond hairs. It was firm and on section it was composed of yellow tissue containing numerous streaks of white tissue. In one zone the mass contained a cyst 2 cm. in diameter. The cyst was filled with cheesy material and pale hairs. One pole of this mass was covered by a sheet of gray-brown and fatty tissue varying in thickness from 0.3 to 1 cm. This tissue was said to have been removed from the mediastinum. The mass was attached to this encapsulating tissue. The parenchyma of the upper lobe was extremely solid. It had a mottling of yellow, cream, tan, and brown areas. There was accentuation of the interlobular septa. The pulmonary tissue was atelectatic in many places. The lower lobe was poorly aerated, though it was not as dense as the upper lobe. The lobular markings were not as prominent. The parenchyma varied from tan to brown.

Microscopic Description.—The rounded mass which filled the cavity in the lung was composed of dense fibrous tissue covered on one aspect by cornified stratified squamous epithelium. In the fibrous tissue were nests of adipose tissue, and under the epithelium were hair follicles and numerous large sebaceous glands. Lymphocytes, plasma cells, macrophages, and a few polymorphonuclear cells were scattered throughout the fibrous stroma. The cystic portion of the mass was lined also by cornified stratified squamous epithelium. Sebaceous glands were also present. In addition, there was a large group of glands in a lobular arrangement around the cyst. These glands consisted of dark and light-staining columnar cells arranged in acinar groups, that communicated with tubular structures lined by a single regular layer of tall pale cells. This zone represented serous and mucous salivary gland elements.

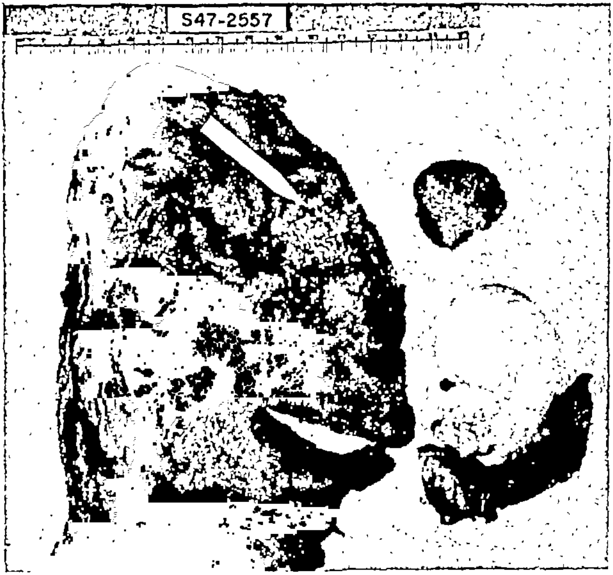

Fig. 2.—Gross section after pneumonectomy showing: Grumous material of the dermoid on the mediastinal surface of the lung and the more solid material and hair which was removed from the cavity in which the dermoid was developing.

The lung tissue which lined the cavity had a layer of granulation tissue on the inner surface. The granulation tissue consisted of young fibrous tissue, numerous small blood vessels, lymphocytes, plasma cells, macrophages, giant cells, and polymorphonuclear cells. Fragments of stratified squamous epithelium were scattered on the surfaces of the granulation tissue. The lung parenchyma showed profound changes; no normal lung tissue remained in this zone. There was severe and extensive fibrosis of the interstitial and interlobular tissue; there was severe distortion of alveoli with dense infiltrates of lymphocytes, plasma cells, macrophages, and giant cells in the interstitial tissue and in the alveolar walls. Polymorphonuclear cells were also present in some areas. The macrophages were full of fatlike material; macrophages commonly filled alveoli. Some of the giant cells had vacuoles and clefts within their cytoplasm. In regions more distant from the site of the tumor the alveoli contained blood and serum, and the bronchi contained a polymorphonuclear exudate. The interstitial tissue in general was increased, particularly in the interlobar and interlobular septa. The changes in the lower lobe varied in intensity, generally the interstitial scarring was present and the inflammatory reaction in the alveoli was represented by blood serum and macrophages.

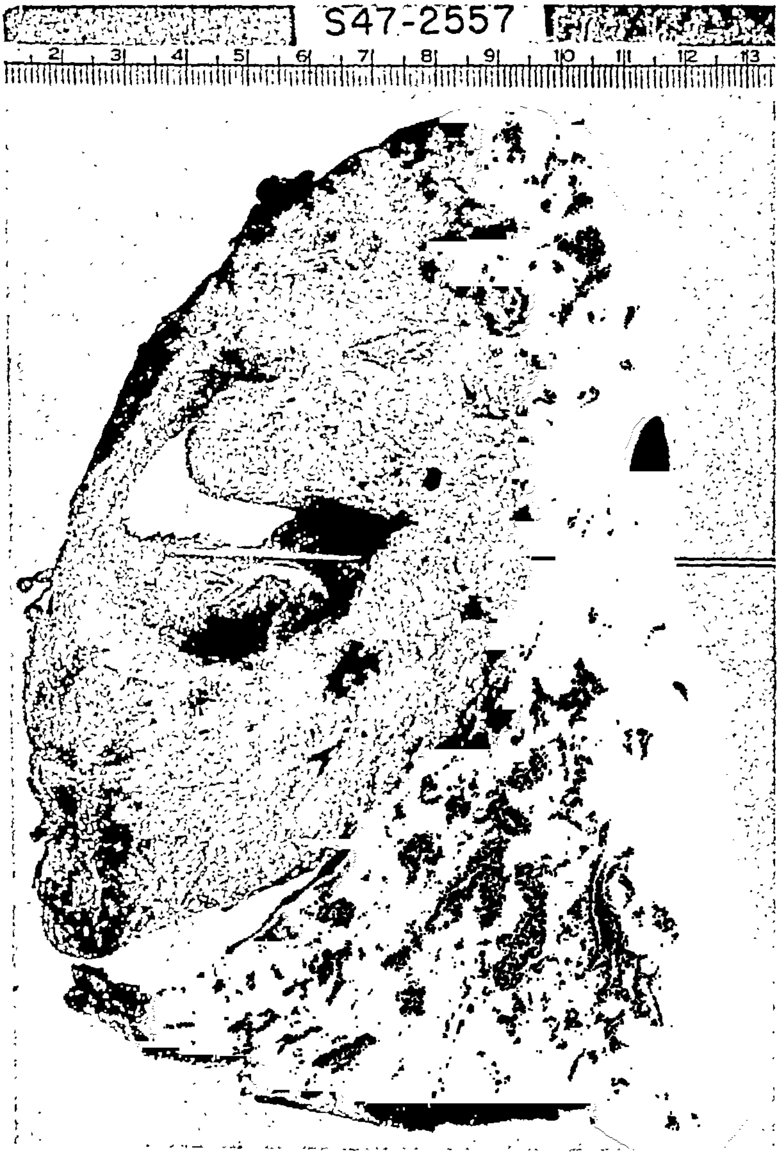

Fig. 3.—Gross cut section of the lung showing the pressure defect in the upper lobe simulating a cavity made by the dermoid with a probe passing from the cavity directly into the left upper lobe bronchus.

A section that represented the bronchus that was traced into the cavity showed a dense chronic inflammatory infiltrate in the bronchial mucosa and surrounding interstitial tissue. The columnar epithelium of the bronchus changed into stratified squamous epithelium; beneath this epithelium were sebaceous glands.

The hilar and mediastinal lymph nodes were enlarged. They had prominent follicles with distinct germinal centers. The sinusoids were lined by many layers of endothelial cells. The sinusoids contained lymphocytes, neutrophiles, eosinophiles, macrophages, and some giant cells. Large and small vacuoles were scattered throughout sinusoids of the lymph nodes.

Fat stains were prepared of the lung and lymph node. With the Scharlach R stain, red droplets were present in the pulmonary parenchyma in the region of the tumor. The fat droplets were very small in the macrophages, in the alveoli, and in the columnar epithelial cells of the bronchi of that region. The fat droplets were larger in the interstitial tissue where they may be engulfed by giant cells or free in the fibrous elements. Here they had the appearance noted in the original biopsy.

There was less fat in the interstitial tissue of the lower lobe and practically none in the alveoli of that lobe. The same blocks of tissue were also stained with osmic acid and the preparations are compared with the Scharlach R stain. It was noted that the droplets that stained red with Scharlach R were also stained black with osmic acid. There was no apparent difference in the quantity of fat demonstrated by the two techniques. Fat droplets were demonstrated in the lymph nodes by these two techniques.

DIAGNOSIS*

1. Dermoid tumor of mediastinum, situated in upper lobe of left lung, communicating with major bronchus.
2. Chronic patchy organizing pneumonitis, left lung, with interstitial scarring due to lipoid from dermoid tumor.
3. Reactive hyperplasia of regional lymph nodes with lipoid in sinusoids.

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* Gerson R. Biskind, Pathologist.

ACUTE PUTRID ABSCESS OF THE LUNG

VI. The Late Results of Surgical Treatment

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During the decade prior to World War II, members of our Thoracic Group at The Mount Sinai Hospital published a series of papers concerning various aspects of putrid pulmonary abscess.[1-18] We, among the participants, described the technique of one-stage drainage in the acute phase of the disease and reported the results derived therefrom.[7, 8, 9, 10, 12] At the time, we summarized our experiences by stating that (1) "cure is achieved without hazard in the great preponderance of cases," and (2) "the results are excellent, not only as to recovery from operation but also as to complete and early restoration of health." The foregoing statements were based upon follow-up observations which, at the time, varied from 3½ months to 10 years in duration.

The passing years have afforded us an opportunity to observe many of our patients for much longer periods; and it is now our purpose to set forth the late results of operation in order to demonstrate that they are not quite as satisfactory as we had assumed originally. This will be done by reviewing briefly the cases of acute putrid pulmonary abscess that we subjected to one-stage drainage prior to Jan. 1, 1945. Up to that date, we had a total of 165 such cases but we shall confine our analysis only to those that could be followed for at least 5 years after operation. It is our opinion that if one adheres to certain strict criteria of "cure," such a long period of follow-up is not essential in order to make certain that the patient will remain well. However, since this communication deals with "late results," we have arbitrarily selected 5 years as the minimum period of observation of all cases to be included in our report.

Among our 165 patients, 154 were operated upon in the "pre-penicillin era." There were 4 operative deaths in our series. The latter, constituting an operative mortality rate of 2.43 per cent, have been reported elsewhere.[12] Of the 161 patients who survived operation, 46 could not be followed for the required minimum period of 5 years and therefore have been eliminated from further consideration. (Of these 46 patients, 4 are known to be dead. One died following an operation for strangulated hernia and 2 died of malignant disease of the pancreas and colon, respectively. The fourth patient died of lobar pneumonia more than a year after the operation for pulmonary abscess. All 4 patients were free of symptoms of pulmonary abscess at the time of death and, in each instance, the latter was due to a cause unrelated to the original pulmonary infection. The remaining 42 patients gradually disappeared from observation. When last seen all were free of symptoms, some having been followed for more

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From the Surgical Service of Dr. Arthur S. W. Touroff, The Mount Sinai Hospital.

Read (by title) at the Twenty-eighth Annual Meeting of The American Association for Thoracic Surgery at Quebec, Canada, May 31, June 1, 2, 1948.

than 4 years after operation.) After eliminating the 4 operative deaths and the 46 cases that could not be followed for the required minimum period of 5 years, 115 cases remained. These cases, which were observed for 5 to 25 years, form the basis for certain conclusions that will be presented at another point. We have divided the cases into two groups, according to certain strict criteria.

Group A consists of patients whom we consider "cured." In order to be classified under Group A, the patient must (1) be entirely symptom-free, (2) have a healed wound, and (3) have a normal chest film or bronchogram. There were 100 patients (86.9 per cent of the 115 cases) in this group. Four have been followed for 20 to 25 years, 7 for 15 to 20 years, 12 for 10 to 15 years, and 77 were under observation for 5 to 10 years.

Group B is comprised of those patients who, in the light of the criteria of "cure" enumerated in the preceding paragraph, cannot be considered "cured" despite the fact that most of them became free of symptoms of pulmonary abscess soon after operation. In this group, there were 15 patients (13.04 per cent of the 115 cases). On x-ray examination, all presented either a small residual pulmonary cavity or persistent pulmonary infiltration. On bronchography, varying degrees of bronchial dilatation were noted in all, but it is to be emphasized that *none* of them presented symptoms of residual pulmonary suppuration. *Nine became entirely symptom-free shortly after operation and have remained so.* The remaining 6 patients either have, or have had in the past, recurring episodes of hemoptysis. One patient, who has been entirely free of symptoms since operation, has had a small persistent bronchocutaneous fistula.

The 15 patients in Group B serve to re-emphasize a viewpoint that we expressed many years ago, namely, that *regardless of absence of evidence of pulmonary suppuration a patient who has had a pulmonary abscess cannot be considered well unless the x-ray film discloses complete disappearance of pulmonary infiltration.*[17] As mentioned already, 6 of our 15 patients have suffered recurrent small hemoptyses. These cases have been observed for 7 to 16 years. It is important to note that while 3 patients developed hemoptysis shortly after operation, the remaining 3 *did not begin to bleed until some years after operation.*

Careful analysis of the histories of the 6 patients, who developed hemoptysis, disclosed that one bled occasionally during the 7 years that we were able to follow him after operation. The second patient has had identical manifestations for 16 years. The third patient had occasional hemoptysis for the first 8 years and has remained well for the past 6 years. The fourth patient was entirely free of symptoms for 4 years and has bled, from time to time, during the past 3 years. The fifth patient was well for 5 years, then had recurrent hemoptysis for 2 years and has been well for the past year. *The last patient was well for 10 years but, during the last 4 years, has had recurrent small hemoptyses.*

Of the 9 patients who remained symptom-free following operation despite the fact that their x-ray films were abnormal, 1 has been followed for 7 years, 2 for 8 years, 2 for 9 years, 2 for 14 years, 1 for 21 years, and the last for 22 years. *In view of the fact that certain of the patients mentioned in the pre-*

ceding paragraph did not commence to bleed for a number of years after operation, there is no assurance that these 9 patients will not have hemoptysis in the future. Bronchography has been performed in all 9 cases and, in each instance, demonstrates the presence of bronchial dilatation of varying degree and extent. In view of the already-demonstrated tendency of such patients to bleed, *a guarded prognosis must be given in all* regardless of the fact that all of them have remained well for 7 years or longer.

With the object of attempting to determine the factors responsible for the persistence of pulmonary cavities or bronchiectasis following drainage of an acute putrid pulmonary abscess, the 15 cases of Group B were reviewed. In each instance, operation was performed within 10 days to 5 weeks of the onset of symptoms; and, accordingly, chronicity of the pulmonary abscess can be excluded as a cause of the residual pulmonary abnormality. The first apparently significant finding was that in 8 patients the abscess cavity, at operation, was noted to be three inches or more in diameter. In 2 of these cases, profuse hemoptysis occurred prior to operation; and, at operation, the cavity was found to measure more than four inches in diameter. In practically all patients with large cavities, the clinical course was characterized by high fever, prostration, and apathy or other evidence of severe toxemia. In 3 cases which presented such clinical features, the preoperative film disclosed very extensive pulmonary infiltration but, at operation, the pulmonary abscess did not exceed two inches in diameter. In another 2 cases in which dense shadows were noted in the preoperative roentgenogram, at operation the lesion was found to have already perforated into the pleura. In these 2 instances, several revisions of the operative wound and prolonged drainage were required. In only 1 case of the 15 was the cavity small (three-fourth inch in diameter) and the preoperative manifestations mild. This patient has remained symptom-free for 7 years since operation, but the postoperative bronchogram revealed varicose dilatation of the branches of the left lower lobe bronchi in the vicinity of the original pulmonary abscess. From all of the foregoing, it appears that cases characterized preoperatively by extensive pulmonary excavation, profuse hemoptysis, and severe symptoms are likely to be complicated postoperatively by persistence of pulmonary cavitation or bronchiectasis, or both. These may occur regardless of the fact that operation is performed at a relatively early stage of the disease.

From a practical standpoint, the question arises whether the cases which we have just discussed might have been treated more effectively by some method other than that employed. In this connection, it is to be emphasized that all but 11 of our patients were treated prior to the time that penicillin and other antibiotics became available to us. Without burdening the reader with a mass of statistics, it may be stated that many a patient with a large acute pulmonary abscess who presented a fulminating preoperative clinical course (hyperacute abscess) made an uneventful convalescence and has remained entirely well for many years following simple surgical drainage.[12] On the other hand, we have presented evidence to indicate that other cases of the same general type, although relieved of symptoms of pulmonary suppuration after operative drainage, may be left with pulmonary cavities or bronchiectatic dilatations which later are a source of hemoptysis. As regards primary lobectomy or segmental resection, we are unaware of any reports in the literature concerning such treatment in a large series of cases of "hyperacute" putrid pulmonary abscess, during the period in which we treated such cases by "one-stage drainage." Accordingly, we are unable to state the mortality, morbidity, and incidence of satisfactory results that might have followed pulmonary resection under the circumstances outlined previously.

Among 154 cases of acute putrid pulmonary abscess operated upon by us *in "the pre-penicillin era" (prior to January, 1943), 41 were of the "hyperacute"* variety. Three of our 4 operative deaths occurred in this group.[12] Thus, simple drainage of these fulminating lesions resulted in a mortality rate of 7.3 per cent prior to the advent of modern antibiotic therapy. All 41 patients suffering from "hyperacute" abscess were so ill at the time of operation, that it seems unlikely that they could have withstood any procedure other than a rapidly performed, emergency drainage under local anesthesia. Specifically, we maintain that lobectomy or segmental resection would have resulted in greater morbidity or mortality than that which resulted from drainage.

Since the advent of antibiotics, there has been a general tendency on the part of surgeons to treat chronic pulmonary abscess by means of resection rather than drainage. There also has been a parallel trend in the treatment of acute putrid abscess of the lung. Up to the present writing, however, we have not encountered any reports of combined pulmonary resection and antibiotic therapy in the treatment of a substantial number of cases of "hyperacute" abscess. Thus, the results of such therapy in "hyperacute" cases still remain in doubt although the results in less severe cases appear to be excellent, not only as regards low morbidity and mortality but also high incidence of cure. For the time being the following mode of treatment of fulminating cases of acute putrid pulmonary abscess appears most logical:

a. In cases in which intensive antibiotic therapy does not result in prompt fall of temperature, reduction of the amount of sputum, and diminution of toxic manifestations, the safest procedure appears to be one-stage drainage. Should the pulmonary cavitation or bronchiectasis persist, secondary lobectomy or segmental resection should be performed at a later date, namely, when the element of gross infection has been eliminated.

b. In cases in which antibiotic therapy results in prompt control of infection, primary lobectomy or segmental resection appear to be the methods of choice.

SUMMARY AND CONCLUSIONS

Prior to Jan. 1, 1945, the authors subjected 165 patients suffering from acute putrid pulmonary abscess to operation; 154 of these cases were operated on in the "pre-penicillin" era.

Operation consisted of drainage in one stage, according to a technique described previously.

Among the 165 cases, there were 4 operative deaths (an operative mortality rate of 2.43 per cent).

Of the 161 survivors, 46 could not be followed for a minimum period of 5 years and therefore were eliminated from further consideration.

One hundred fifteen cases, followed for from 5 to 25 years, form the basis of this report.

The 115 cases were divided into two groups, according to strict criteria.

Group A consists of patients who are considered "cured." They are free of symptoms, have healed wounds, and have negative chest films or bronchograms. There are 100 patients in this group (86.9 per cent of 115 cases).

Group B consists of patients who cannot be considered well because of the fact that they have *residual postoperative pulmonary cavities or bronchiectasis.* There are 15 cases in this group (13.04 per cent of 115 cases). *None of them has symptoms of residual pulmonary suppuration. Nine have been entirely symptom-free.* The remaining 6 patients have had hemoptysis at one time or another. Because, in some cases, bleeding occurred quite a number of years after operation, it is conceivable that the 9 patients who have been free of hemoptysis may bleed in the future. Under any circumstances, 13.04 per cent of 115 cases of acute putrid pulmonary abscess cannot be considered "cured," following one-stage drainage. This is a higher incidence of unsatisfactory results than we had assumed previously on the basis of a shorter period of follow-up observation.

Practically all patients in Group B presented large abscesses, extensive areas of pulmonary infiltration, profuse hemoptysis, or severe clinical symptoms, prior to operation.

Among the 165 cases, 41 were of the above-mentioned "hyperacute" type. One-stage drainage in these 41 cases resulted in 3 operative deaths (an operative mortality rate of 7.3 per cent). However, the majority of patients suffering from "hyperacute" abscess responded well to the one-stage drainage procedure.

While primary lobectomy or segmental resection constitute theoretically ideal procedures in cases of "hyperacute" abscess, in so far as they would appear to eliminate the danger of residual pulmonary cavitation and bronchiectasis, it seems fair to assume that such radical surgery would have been attended by a significantly higher morbidity and mortality than followed the one-stage drainage operation before the advent of antibiotics.

Since the advent of antibiotics, the ideal appears more capable of being achieved.

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TRANSTHORACIC, THORACOABDOMINAL PORTACAVAL ANASTOMOSIS

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THE subject of portal cirrhosis has interested both internist and surgeon for many years. The prognosis in this condition has always been poor; death has been uncomfortably drawn out or has come with dramatic suddenness, accounted for by one or any combination of the following mechanisms:

- A. Liver failure (cholemia)
- B. Portal hypertension
  - 1. "Wasting ascites"
  - 2. Exsanguination, due to rupture of:
    - (a) Esophageal varices
    - (b) Gastric varices

The treatment of depressed liver function is medical. Remarkable improvement is generally obtained with a regime consisting of a high protein, high carbohydrate, low fat diet, lipotropic substances, supplementary vitamins and proteins, liver extract, etc. The problem of portal hypertension, on the other hand, is one of mechanics. Due to intrahepatic, periportal fibrosis, congestion in the portal system ensues. Thereafter, the increased intravenous hydrostatic pressure may cause ascites, or compensation may take the form of varicosities of the venous tributaries, particularly the esophageal and gastric network. More commonly ascites and varicosities coexist.

The methods devised to combat the disastrous sequelae of portal hypertension are numerous and ingenious. These include the Talma-Morison operation,[1, 2] insertion of the Crosby-Cooney button,[3] sclerosing of the esophageal varicosities,[4, 5] intraesophageal venous tamponage,[6] posterior mediastinotomy,[7] gastric resection,[8] and gastroesophagectomy.[9] Such methods, however, fail to strike at the critical point of obstruction, and are at best either partially or temporarily effective. The shunting of blood from the portal system directly into the systemic venous circulation is the most rational and effective method of dealing with portal hypertension. This method was proposed by von Eck in 1877,[10] and subsequently tried on human beings with varying and questionable success by Tansini (1902), Vidal (1903), De Martel and Lenoir (1910), Rosenstein (1911).[11] It remained, however, for the stimulating work of Whipple,[11, 12] and of Blakemore and Lord,[13, 14, 15] to renew interest in the concept of supplementing the collateral circulation between the portal and systemic venous systems, and to establish this therapy as one of choice in the management of portal hypertension.

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Portal hypertension may be due to an intra- or extrahepatic block. The incidence of intrahepatic block, notably portal cirrhosis, exceeds by far the relatively few cases of extrahepatic block which are generally due to thrombosis, scarring, or cavernomatous transformation of the portal or splenic veins.[16] In cases of extrahepatic block, a splenorenal shunt is indicated. In portal cirrhosis, however, either a splenorenal or a portal-inferior vena cava (Eck fistula) anastomosis is available. It is generally conceded that the Eck fistula procedure is more desirable.[12, 14, 17] In the first place, and most important, it is capable of shunting more blood than a splenorenal anastomosis. Normally, the splenic vein handles approximately 20 to 40 per cent of the total blood volume of the portal system. Splenorenal shunt, therefore, permits only a partial reduction in portal hypertension, generally between 100 and 150 mm. of water[14] and while such a drop may be sufficient in some cases to alleviate symptoms, closer approximation to the normal portal pressure of 100 mm. of water is desirable when dealing with abnormal pressures ranging between 350 and 600 mm. of water.

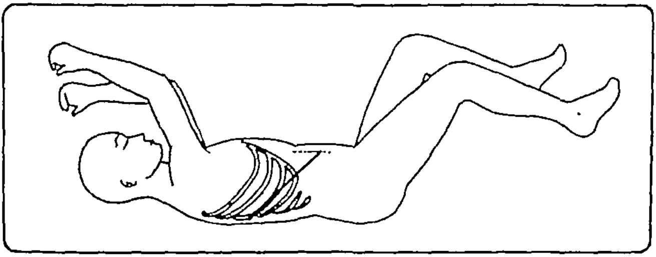

Fig. 1.—Position of patient and line of incision. The patient lies on the left side in the true lateral position. The incision is made directly over the ninth rib commencing at the lateral margin of the right erector spinae muscles and is continued onto the abdomen to the lateral border of the right rectus muscle.

A second objection to splenorenal shunt for portal cirrhosis is the greater likelihood of thrombus formation at the site of anastomosis. To offset this complication, heparin is generally employed postoperatively, a precaution beset with great hazard. Finally, splenorenal shunt is not as well tolerated by the patient as is an Eck fistula. The majority of cases of cirrhosis of the liver are associated with splenomegaly[18]; perisplenitis is the rule and the splenectomy which is a necessary preliminary to splenorenal shunt is accomplished with difficulty, if at all. A considerable number of cases of splenectomy in lieu of a proposed shunt operation never reach the literature, and fatal outcomes in these instances are listed as failures in splenectomy and not splenorenal shunts.

The objection of by-passing the liver with portacaval shunt (Eck fistula) on the grounds of possible nutritional difficulties[19] does not seem a valid one. McIndoe[20] demonstrated that in portal cirrhosis the maximum amount of blood reaching the liver via the portal vein is 13 per cent. The establishment of a splenorenal shunt will reduce even this amount to a negligible figure, even though the portal vein itself is not molested. Moreover, Herrick[21] has shown by his perfusion studies that in the normal liver there is a 1 mm. rise in portal vein pressure for every 40 mm. rise in hepatic artery pressure, while in the cirrhotic liver the ratio is reduced to 1:6. Herrick further pointed out that an arterial rise in pressure does not affect the portal pressure in normal livers until the 100 mm. mark is passed, whereas in cirrhotic livers the influence is discernible with pressures as low as 30 mm. Such increased sensitivity of portal tension to hepatic artery alterations in pressure is another point in favor of portacaval as opposed to splenorenal shunt. It is, therefore, evident that the Eck fistula offers the greatest possible relief of portal hypertension and should be employed in all but those cases in which other types of shunt operations are specifically indicated, such as the splenorenal[15] and combinations of the superior and inferior mesenteric with the vena cava, left ovarian, and left adrenal veins as reported by Linton.[22] In general, it would appear that the chief deterrent to the widespread adoption of the Eck fistula is the fact that when the usual abdominal approach is employed, it is a technically difficult procedure.

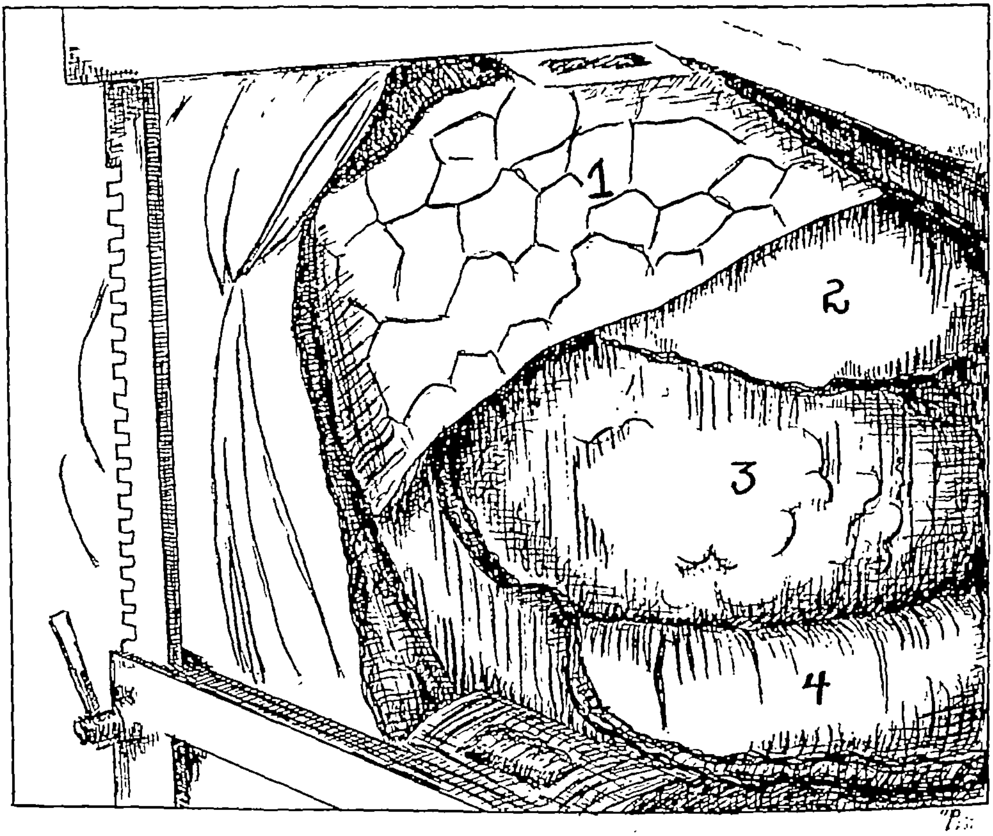

Fig. 2.—Exposure following resection of ninth rib: *1,* Lower lobe of right lung; *2,* upper leaf of incised diaphragm; *3,* liver; *4,* lower leaf of diaphragm.

In an effort to simplify portal-inferior vena caval anastomosis, one of us (V. P. S.) has reported a transdiaphragmatic, thoracoabdominal approach.[23, 24] This method not only facilitates exposure and obviates the need of working under the costal cage in a deep wound, but permits access to the portal vein to one side, instead of behind the common duct and hepatic artery. Briefly, the procedure is carried out as follows:

The patient is placed on the left side, in the true lateral position; a sand bag elevates the left loin. An incision is made over the ninth rib, commencing at the lateral border of the right erector spinae muscles and extending to the lateral margin of the right rectus muscle. The ninth rib is resected subperiosteally, from its angle to the costochondral juncture, which is severed. (The ninth interspace may be used.) After the chest is opened, the diaphragm together with the abdominal musculature and peritoneum are cut along the line of incision, thereby freely uniting the thoracic and abdominal cavities.

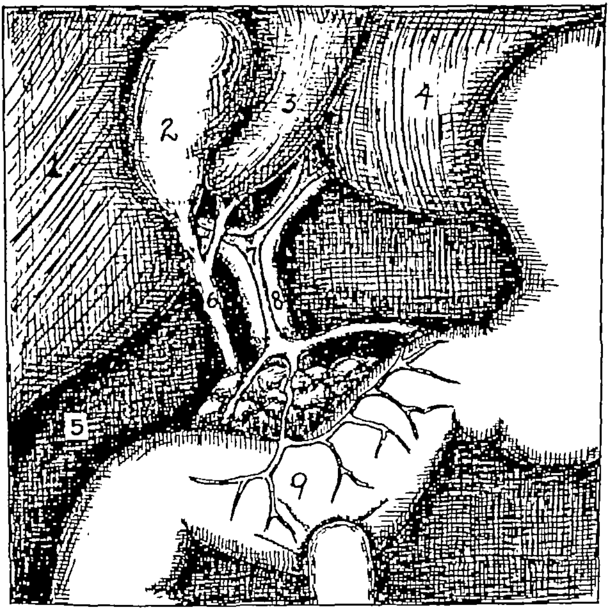

Fig. 3, A.

Fig. 3, A and B.—Schematic drawings comparing the relationship of the structures in the hepatoduodenal ligament as viewed from the prone (anatomic) position and the left lateral position.

A. Prone position (abdominal approach). The portal vein lies behind the common duct and hepatic artery: *1*, Right lobe of liver; *2*, gall bladder; *3*, quadrate lobe of liver; *4*, left lobe of liver; *5*, site of inferior vena cava; *6*, common bile duct; *7*, hepatic artery; *8*, portal vein; *9*, retracted duodenum exposing pancreas above.

The lung and intestines are packed away and the liver is dislocated into the right hemithorax, bringing the hilum of the liver and the inferior vena cava into direct view; handling of the intestines is minimal, thereby lessening the likelihood of postoperative ileus. The peritoneum over the inferior vena cava is incised, and the inferior vena cava is mobilized from the level of the liver to the entrance of the right renal vein. Attention is then directed toward mobilization of the portal vein.

It is wise to begin dissection of the portal vein laterally, so as to avoid injury to the common duct. Complete mobilization of the portal vein is required, from its origin at the superior border of the pancreas to the points where its right and left branches enter the substance of the liver. Ligatures are placed around each branch and the main vessel is placed between the jaws of a Blalock clamp. At this time, pressure readings of the portal vein are taken, following which the Blalock clamp is tightened. The branches of the portal vein are then ligated. A transfixion ligature is placed at the site of bifurcation, and the portal vein severed transversely just below this ligature, ensuring the greatest possible length of portal vein. Traction on the portal vein now facilitates its complete mobilization.

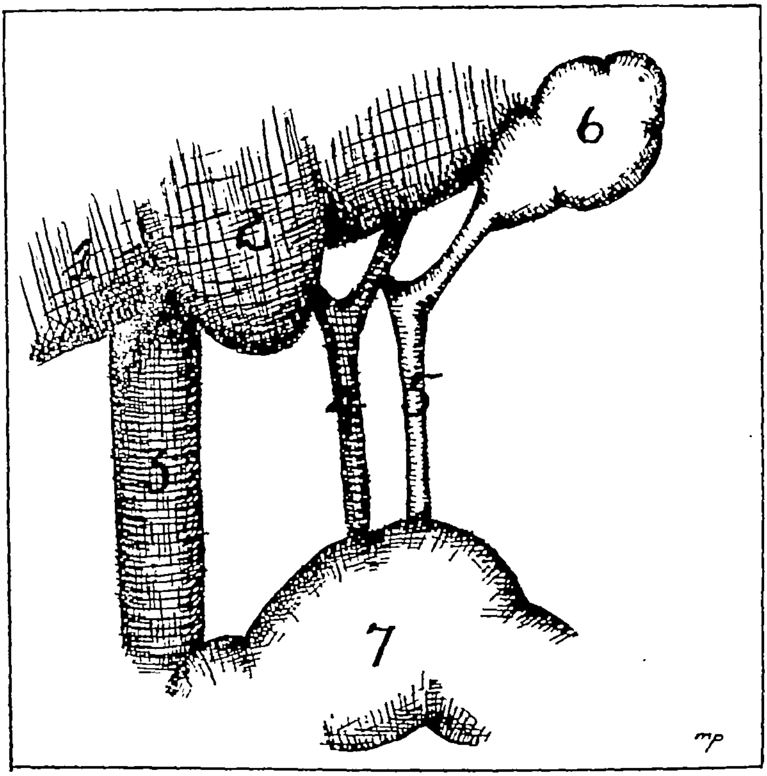

Fig. 3, *B*.

Fig. 3, *B*.—Left lateral position (thoracoabdominal approach). The portal vein now lies to one side of the common duct and hepatic artery; the common duct obscures the hepatic artery from view: *1*, Right lobe of liver; *2*, the caudate lobe of liver now comes into view; *3*, inferior vena cava; *4*, portal vein; *5*, common duct overlying the hepatic artery; *6*, gall bladder now lying to the right; *7*, duodenum.

The inferior vena cava has already been prepared for anastomosis. Since this vessel may not be clamped off above the level of the renal vessels for more than ten minutes without incurring anuria, it is necessary to permit vena caval blood flow during the anastomosis. This is made possible by merely constricting a portion of the anteromedial wall of the vessel by an unshod special clamp.* The pinched-off portion of the vessel is utilized for the anastomosis while blood flow beneath the horizontal blades of the clamp continues freely. A portion of the vein held in the clamp is then excised, the length of excision corresponding with the width of the severed portal vein. Excision of a portion of the vein is to be preferred over simple incision; the musculo-elastic fibers in the media of the inferior vena cava run longitudinally, and, if simply incised, would tend to reapproximate the wound. Since a transverse incision is not feasible, the removal of a small portion of the wall of the inferior vena cava insures against postoperative closure of the anastomosis. To facilitate this maneuver, a special long-handled scissors with a large, upward curve has been devised.*

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*The Satinsky clamp and scissors are manufactured by George P. Pilling & Sons, Philadelphia, Pa.

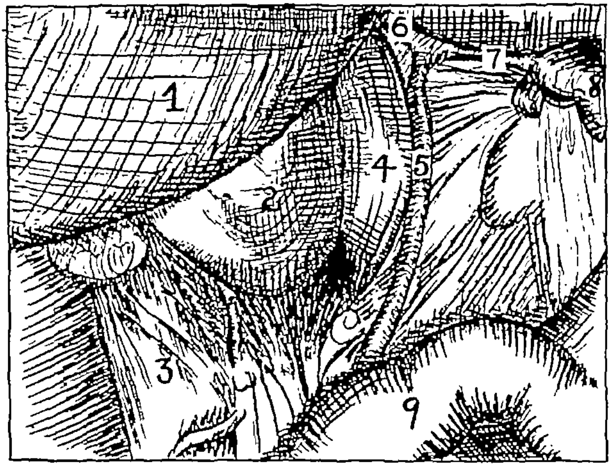

Fig. 4.—Following retraction of the liver and intestines, the operative area is exposed. 1, Retractor over inferior surface of right lobe of liver; 2, caudate lobe of liver; 3, inferior vena cava; 4, portal vein; 5, common bile duct; 6, hepatic duct; 7, cystic duct; 8, gall bladder; 9, duodenum.

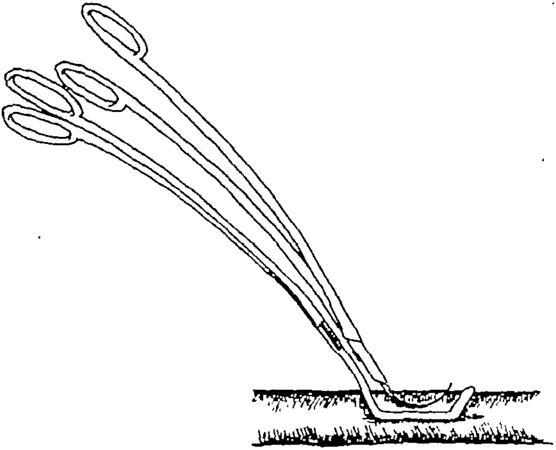

Fig. 5.—Satinsky clamp and scissors. The inferior vena cava is clamped in a manner that permits venous flow during the performance of the portacaval anastomosis. The special curve of the scissors facilitates excision of a portion of the inferior vena cava.

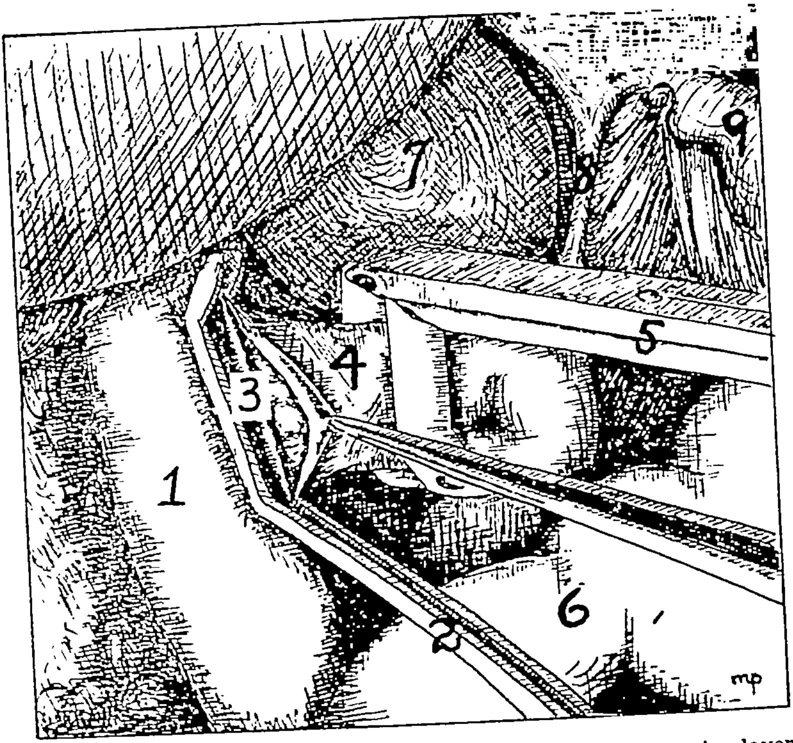

Fig. 6.—Clamps control portal vein and inferior vena cava as posterior layer of anastomosis is completed. *1*, Inferior vena cava; *2*, Satinsky clamp; *3*, posterior suture line; *4*, portal vein; *5*, Blalock clamp; *6*, duodenum; *7*, caudate lobe of liver; *8*, common bile duct; *9*, gall bladder.

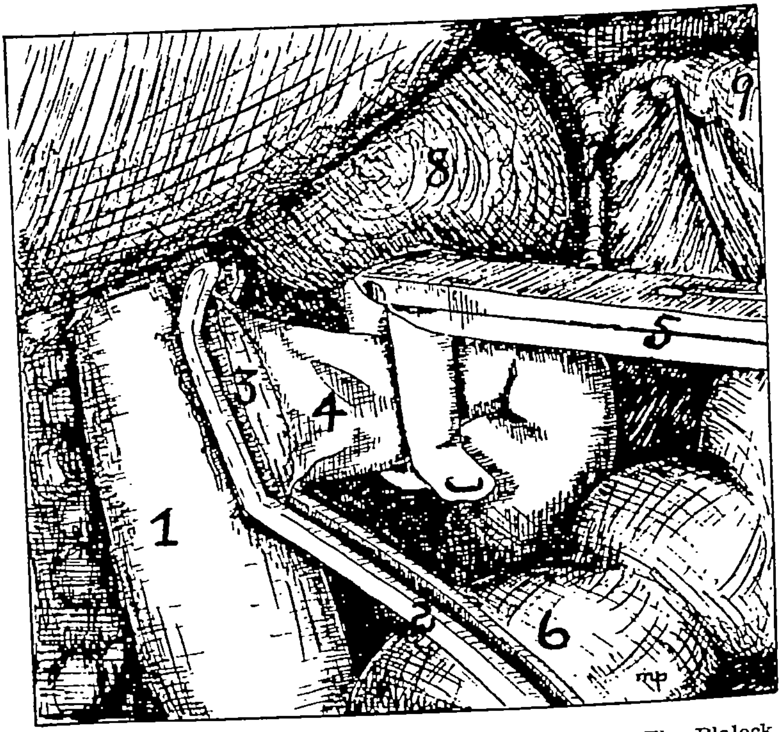

Fig. 7.—Anastomosis is completed with clamps still in place. The Blalock clamp will be released first. *1*, Inferior vena cava; *2*, Satinsky clamp; *3*, anterior suture line; *4* portal vein; *5*, Blalock clamp; *6*, duodenum; *7*, common bile duct; *8*, caudate lobe of liver; *9*, gall bladder.

Direct anastomosis of the proximal end of the divided portal vein to the side of the inferior vena cava is performed with 00000 braided silk on an atraumatic needle. A running everting mattress suture is used. The sutures are not intermittently interrupted as suggested by Blalock.[25] Instead, a knot is tied at the starting and end points of the posterior suture line to prevent purse stringing of the vessel. Both knots are tied on the outside. An interrupted stay suture unites the portal vein and inferior vena cava on either side of the suture line to relieve some of the tension at the angles of the anastomosis and to prevent the angles from pulling in. One of the free ends of the tension sutures is tied to a free end of the anastomotic sutures. Until the completion of the anastomosis, the intima of both vessels are frequently irrigated with a dilute heparin-saline solution.

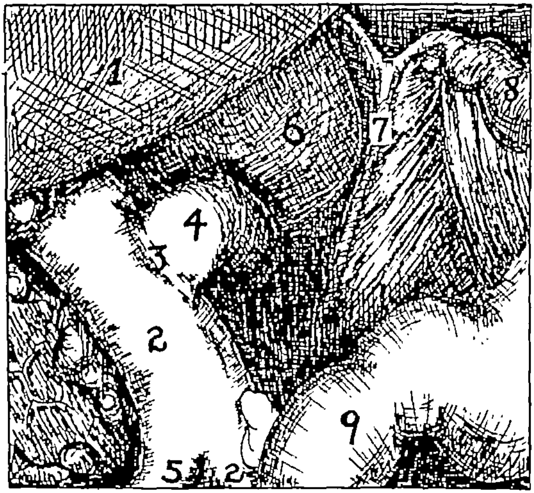

Fig. 6.—End-to-side, intima-to-intima anastomosis of the portal vein to the inferior vena cava; *1*, Retractor over right lobe of liver; *2*, inferior vena cava; *3*, suture line; *4*, portal vein; *5*, right renal vein; *6*, caudate lobe of liver; *7*, common duct; *8*, gall bladder; *9*, duodenum.

Note position of suture line after release of clamps; the anastomosis occupies the anterior aspect of the inferior vena cava in a plane exceeding 90° relative to the right renal vein. There should be neither angulation or tension.

When the anastomosis is completed, the Blalock clamp is removed. This permits venous blood to fill up the interstices made by the sutures. Unless there is a large leak in the suture line requiring additional, interrupted sutures, the oozing will stop in a few moments. The clamp on the inferior vena cava then may be removed, and the efficiency of the shunt at once becomes visible. Penicillin is placed in the peritoneal and thoracic cavities (50,000 units into each), the diaphragm is sutured with imbricating, interrupted mattress sutures, and the abdomen and chest are closed in layers. At the Thoracic Surgical Unit of the Hahnemann Hospital, closure of the chest with intercostal drainage is the rule. Cotton suture technique is employed.

Because of the large size of the shunt, the fact that the portal tension is highest and the inferior vena caval pressure lowest at the site selected for anastomosis, and because a portion of the inferior vena cava is excised, there need be no fear of either postoperative closure or thrombus formation at the site of anastomosis. For this reason heparin is not employed postoperatively. Consequently, not only are the dangers of anticoagulant therapy avoided, but early ambulation is made possible.

An objection to the transthoracic route for portacaval shunt may be raised by those who argue the need for pressure readings of the portal system at the time of operation. Generally, a diagnosis of intra- or extrahepatic block can be made preoperatively. Indeed, at the present time, a good many patients have been found to have portal cirrhosis at a previous laparotomy. In any case, if pressure readings are desired, the abdominal portion of the wound can be made first, and the incision can be extended to the left instead of over the right costal cage, if a splenorenal shunt is specifically indicated. The use of a tilt table facilitates this maneuver.

CASE REPORTS

CASE 1.—E. G., male, aged 44 years, had enjoyed excellent health until he developed diabetes mellitus in 1940. Then, in January, 1946, the patient vomited blood and passed many tarry stools. A diagnosis of duodenal ulcer was made and purportedly confirmed by x-ray examination. An episode of hematemesis occurred eight months later and again in January, 1947. A splenomegaly was noted but apparently little significance was attached to this finding.

When the patient was first seen by one of us attention was focused upon the splenomegaly. Although the liver function tests were well within normal limits with the exception of the Bromsulphalein test, which showed 19 per cent retention, a diagnosis of cirrhosis of the liver was tentatively made.

In May, 1947, a laparotomy was performed. Cirrhosis of the liver was found, with marked splenomegaly; a biopsy of the liver was taken and a Talma-Morison procedure carried out. The presence of a duodenal ulcer was not demonstrated. The patient made an uneventful recovery and the pathology of the liver was reported as conclusive of extensive active portal cirrhosis.

Four weeks later another gastrointestinal hemorrhage took place. This was combated with blood transfusions.

From June, 1947, until January, 1948, the patient remained in poor health. He was maintained on periodic intramuscular injections of liver and 25 units of protamine zinc insulin. At this time the liver function tests were as follows: Total protein 6.4 with 4.2 albumin and 2.2 globulin; cephalin flocculation +1; thymol turbidity 4.3 units; Bromsulphalein 20 per cent retention in one hour; prothrombin time 55 per cent of normal; total cholesterol 250 mg. per cent; cholesterol esters 44 per cent. X-ray examination showed the presence of esophageal varicosities which until this time had not been demonstrated. Barium enema showed the splenic flexure to be sharply depressed by a huge spleen lying above.

A portacaval shunt for the relief of bleeding of esophageal varices which was secondary to an obvious portal hypertension seemed clearly indicated and on Jan. 28, 1948, the shunt was established according to the previously described method. A moderate degree of ascites was found at the time of operation. Convalescence was uneventful. Since operation the patient has enjoyed considerable comfort and there has been no evidence of gastrointestinal bleeding. The spleen is no longer palpable and there is no x-ray evidence of its enlargement. Esophagograms fail to demonstrate varices. As a whole, the liver function tests have remained unaltered. The patient has gained weight and with the exception of the diabetic state, does not consider himself ill or incapacitated.

Comment.—This case represents the ideal for transthoracic portacaval shunt: (1) The patient was in fairly good general condition; (2) liver function tests showed the liver not to be too severely damaged; (3) diagnosis had been unequivocably established; (4) maximum collateral circulation between the portal and systemic systems of veins had long been attained; its inadequacy was manifested by repeated bouts of gastrointestinal hemorrhage, and it appeared certain that only a more efficient collateral pathway, preferably in the form of an Eck fistula, could avert a fatal outcome. At the same time, the clinical manifestations of a decompensating collateral circulation indicated that the liver was obtaining its blood supply almost entirely from a compensatorily dilated hepatic artery, and that it would, therefore, be safe to divide the portal vein; (5) an enormously enlarged spleen together with its highly vascular perisplenitis was left unmolested; (6) adhesions from the previous laparotomy and a previously elective attachment of the omentum to the anterior abdominal wall were completely avoided by the transthoracic thoracoabdominal approach.

In addition to the indications for portacaval shunt and the advantages of the recommended approach, this case emphasizes the desirability of preserving the spleen; congestive splenomegaly and its associated hypersplenism resolved shortly following the establishment of the portacaval shunt.

CASE 2.—A. A., male, aged 54 years, a heavy drinker, was admitted to the hospital in a state of shock one hour following an episode of severe hematemesis. Past history revealed hospitalization two months previously for hematemesis and progressive abdominal enlargement, a forty to fifty pound weight loss in the preceding two years, and variable ankle swelling during the preceding two months.

Significant Physical Findings on Admission.—Blood pressure 90/50, with a pulse rate of 124 per minute; grade 2 aortic systolic cardiac murmur; marked distention of the abdomen with elicitable fluid wave; nonpalpable liver and spleen; spider hemangiomas over the right chest and shoulder; bilateral 2+ ankle edema.

Significant Laboratory Studies.—Red blood cells, 2,000,000 per c.mm. with a hemoglobin of 7.8 grams per cent; white count essentially normal; blood urea nitrogen 28 mg. per cent; chlorides 470 mg. per cent; carbon dioxide combining power 40.0 volumes per cent; serum proteins 7.0 per cent with a 2.8 per cent albumin and 4.2 per cent globulin; Bromsulphalein excretion test 20 per cent retention; cephalin flocculation +2 in 48 hours; thymol turbidity test negative in 18 hours.

Course in Hospital.—Following admission the patient responded to liberal administration of citrated whole blood transfusions and plasma intravenously. He was placed on a high protein diet (200 grams daily), choline 1.0 Gm. three times daily, thiamine hydrochloride 100 mg., nicotinamide 100 mg. and ascorbic acid 500 mg. daily.

On the second, fourth, and sixth hospital days the patient vomited copious amounts of bright red blood; on each occasion he went into shock, but fortunately responded to liberal whole blood and saline infusions. X-ray examination of the esophagus with barium revealed esophageal varices and the patient was scheduled for portacaval shunt. But once again hematemesis supervened. In an attempt to arrest hemorrhage, esophageal tamponade was instituted, without success. Only repeated replacement of the blood loss kept the patient alive. By the eighth hospital day the patient was comatose, markedly icteric, and manifested auricular fibrillation. Blood urea nitrogen was 38 mg. per cent and the carbon dioxide combining power 31.5 per cent. Abdominal paracentesis at this time recovered 3,000 c.c. of amber fluid.

The patient remained in the state of apparent liver failure for seven days then slowly began to improve; laboratory findings returned to normal except for a red blood count of 2,800,000 per c.mm. with a hemoglobin of 7.6 grams per cent; prothrombin level (Quick) 53 per cent; total protein 5.5 with a 2.7 per cent serum albumin and a serum globulin of 2.8 per cent.

Transthoracic portacaval anastomosis was performed 24 days following admission. At operation a small hobnailed liver was demonstrated. During the course of the operation (a 4-hour procedure), the patient received 1,500 c.c. of citrated whole blood and left the operating room in good condition. On the first postoperative day the patient was ambulated and hematologic studies were essentially unchanged from preoperative levels. On the second postoperative day, without warning, the patient experienced a sudden bout of severe hematemesis and despite replacement therapy died in two hours.

Pertinent autopsy findings revealed the portacaval stoma to be inviolate. However, there was marked compression of the portal vein which was, in part, found to be overlying the anterior aspect of the inferior vena cava proximal to the suture line. Other significant findings were a disproportionately enlarged caudate lobe of the liver and severe congestion of the major part of the gastrointestinal tract, with intermittent areas of small ruptured veins. The fatal gastrointestinal hemorrhage was secondary to the marked portal hypertension which followed upon compression of the portal vein. Undoubtedly, it was the preoperative, physiologic connections between the portal and systemic systems of veins which accounted for the forestalling of death until the second postoperative day.

Comment.—In retrospect it was easy to reconstruct the combination of anatomic factors and technical errors which resulted in compression of the portal vein: (1) In this patient the caudate lobe was inordinately enlarged, almost reaching the level of the renal veins. Unfortunately, the portal vein was permitted to overlie the caudate lobe in its new, anastomotic position; we realize now this was a mistake in judgment. But even this factor in all probability would not have had such disastrous effects were it not for the fact that (2) the suture line was established on the same plane as the right renal vein. This means that when the patient was rotated on his back, from the point of view of anatomic position the suture line occupied the true lateral, instead of the desirable anterior or medial aspect of the inferior vena cava. The portal vein, stretched over the inferior vena cava and subjected to an increase in intra-abdominal pressure in the prone position, was, in effect, sandwiched between two resistant forces. Again, if the caudate lobe were not enlarged, it is possible that the poor position of the suture line would not have had such a catastrophic result.

There are several lessons to be learned from this case:

1. A patient can be carried through an operation for portacaval shunt with prothrombin levels just above 50 per cent.

2. In the true lateral position, the inferior vena cava presents its lateral aspect, more or less in the plane of the right renal vein. Care must be taken to establish the anastomosis of the portal vein to the inferior vena cava in the plane 90° to 180° in relationship to the right renal vein; this precaution will guard against "twisting" of the portal vein over the inferior vena cava. The use of a tilt table may be helpful in securing the desirable position for anastomosis. In practice, however, the initially recommended position of the patient presents no real difficulty since the long, curved handle of the Satinsky clamp facilitates easy selection of a site for anastomosis and efficient control of the inferior vena cava.

3. If an enlarged caudate lobe is present, and in Laennec's cirrhosis this is an unusual finding, the transposed portal vein should be placed below this structure so that it can rest unencumbered on all sides. It may be necessary to deliver the portal vein below the pancreas and establish the anastomosis caudal to the level of the renal veins. As an alternative, the hindering portion of the caudate lobe of the liver may be resected.

4. The urgency of surgical intervention in cases of portal cirrhosis with severe hematemesis is emphasized. Undue delay invites repeated bouts of gastrointestinal hemorrhage. The optimal time for surgery is immediately following restoration of blood loss, other factors permitting.

CASE 3.—S. D., male, aged 47 years, was an acknowledged alcoholic who admitted to the consumption of one bottle of whiskey daily; anorexia, thirty-five pound weight loss, and progressive ascites and dependent edema during the two years prior to admission; edema of eyelids, severe dependent edema and ascites commencing eleven weeks before hospitalization, with an incident of coma during this time; repeated abdominal paracentesis.

Positive Physical Finding on Admission.—Emaciation, disorientation; liver edge palpable at the crest of the ileum; marked abdominal distention, and dependent edema.

Significant Laboratory Studies.—Serum proteins 6.1; albumin fraction 2.2 per cent; globulin fraction 3.9 per cent; prothrombin (Quick) 63.5 per cent; cephalin flocculation +3 in 18 hours; thymol turbidity +3; Bromsulphalein 15 per cent retention; blood urea nitrogen 10; chlorides 596.7.

Course in Hospital.—Following admission, patient was placed on a high protein diet (200 grams daily), crude liver 2 c.c. intramuscularly and Mercupurin 2 c.c. daily; Solulexin ampules 1 twice daily and Synkovite 10 mg. daily. Peritoneoscopy revealed a large, moderately nodular and granular liver. Biopsy specimens taken from the liver at this time failed to absolutely reveal the structural cellular pattern of cirrhosis. Despite maximum vigorous therapy, the patient showed no improvement. On the thirteenth day after admission, a transthoracic portacaval anastomosis was performed. The pressure in the portal vein prior to shunt was 400 mm. of H_2O; following anastomosis it was found to be 160 mm. of H_2O. The patient was administered 1,500 c.c. of citrated whole blood through a 3¼-hour procedure, and left the operating room in good condition. The immediate postoperative course presented certain difficulties. The patient was uncooperative and refused to eat. Intravenous protein hydrolosates and whole blood transfusions were employed to maintain protein levels. Abdominal paracenteses were required at weekly intervals; between 2,700 and 5,000 c.c. of amber fluid were withdrawn. Four weeks postoperatively, in addition to dependent edema and ascites, the patient demonstrated a right hydrothorax; thoracentesis recovered 1,200 c.c. of fluid on one occasion and 1,000 c.c. on another. During this time total proteins ranged between 5.0 and 5.9 with albumin levels between 2.3 per cent and 2.2 per cent and globulin values between 2.7 per cent and 3.7 per cent. Approximately six weeks following the establishment of portacaval shunt the patient commenced to show improvement. He was discharged nine weeks following surgery without ascites, edema, or hydrothorax. At this time total protein was 5.3, albumin 3.2 per cent, globulin 2.1 per cent.

Comment.—This case brings out three points worthy of special consideration. (1) A blood serum albumin below 3 per cent is not necessarily a contraindication for portacaval shunt, as generally believed. This patient tolerated surgery well with an albumin of 2.2 per cent. (2) Patients with cerebral manifestations of liver failure in addition to portal hypertension should be operated upon as soon as their general condition permits. We have had instances in which "waiting for the optimal time" following recovery from cerebral involvement finally eventuated in a recurrence of symptomatology with death. We believe that *the optimal time is as soon as possible.* As in this case, patients may continue to go downhill despite adequate medical treatment. Actually, by ordinary standards, this patient was a very poor surgical risk. (3) Following portacaval shunt, ascites and edema may not disappear for several weeks. It is interesting to note that there was very little change in the total protein and albumin-globulin ratios from the time of admission to discharge, certainly not enough to account for the hydrothorax and the subsequent gradual disappearance of the ascites and edema. This observation opens up for conjecture the possible existence of factors other than those already known governing tissue fluid distribution (W. Likoff).[26]

CASE 4.—R. W., aged 22 years, was hospitalized in a profound state of shock following an acute episode of hematemesis. Past history revealed that three years previously, following an attack of hepatitis, a diagnosis of Banti's disease was made. Exploratory laparotomy at that time demonstrated hepatic cirrhosis associated with splenomegaly. For one year before admission there had been intermittent edema of the legs and ankles, and progressive increase in abdominal girth. Four months prior to admission the patient experienced and ignored two bouts of gastrointestinal hemorrhage, expressed orally.

Laboratory Studies on Admission.—Red blood cells, 1,940,000 with a hemoglobin of 5.5 grams per cent; white blood count essentially normal; prothrombin time (Quick) 100 per cent; serum proteins 4.55 per cent with an albumin fraction of 2.91 per cent and a globulin fraction of 1.64 per cent; Bromsulphalein test showed 24 per cent retention of the dye; cephalin flocculation +3 in 48 hours; thymol turbidity was +1 in 24 hours; cholesterol 140.

Course in Hospital.—Pertinent physical findings on admission revealed a pale, apprehensive white man with subnormal temperature. Pulse rate was 134 and the blood pressure barely perceptible at the level of 50 mm. of mercury systolic. He made remarkable recovery with liberal whole blood transfusion. The patient was placed on a high protein diet with supplementary vitamin, liver, and lipotropic preparations. Studies of the esophagus by x-ray examination demonstrated considerable varicosities of the lower esophagus. With repeated blood transfusion a hematologic level of 4,000,000 red blood cells per c.mm. with a hemoglobin of 11.6 grams per cent was finally obtained.

Seventeen days after admission, a transthoracic portacaval anastomosis was performed. Pressure reading in the portal vein prior to anastomosis was 400 mm. of water. At the completion of the anastomosis pressure within the portal vein was 190 mm. of water. The patient was administered 2,000 c.c. of whole blood through the course of a 4-hour procedure and left the operating room in good condition. The postoperative course was uneventful. The patient was discharged on the twenty-first postoperative day, with the edema just beginning to disappear. Liver function studies at the time of discharge showed no appreciable changes.

Comment.—In this case, portal hypertension was clinically manifested by both ascites and gastrointestinal hemorrhage. A normal prothrombin time and an admission serum albumin above the critical level for edema demonstrated that the ascites and hemorrhage were not attributable to factors of depressed liver function; portacaval shunt was the only means of averting unexpected death from rupture of esophageal varices or expected wasting from loss of proteins in ascitic fluid.

SUMMARY

I. *The indications for portacaval shunt* may be summed up as follows:

1. Portal hypertension due to intrahepatic block in which gastrointestinal hemorrhage, ascites, or both threaten the life or comfort of the patient, immediately or in the predictable near future, and in which the hemorrhage or ascites are proved to be due to portal hypertension and not low prothrombin and serum albumin levels.

2. Over-all liver function studies which will offer the patient a fair chance of surviving surgery.
    a. Patients with a prothrombin time of 50 per cent or more will tolerate surgery, from the point of view of a controllable hemorrhage diathesis.
    b. Patients with serum albumin ranging in the low levels of 2.0 per cent will tolerate surgery, from the point of view of depressed liver function. It is naturally expected that every known means be utilized to improve liver function maximumly prior to operation.

3. Cases of intrahepatic portal block in which an enormously enlarged spleen, a previous splenectomy, and/or a previous abdominal laparotomy mitigate against a contemplated splenorenal shunt. These indications are included only for the sake of completeness, since it is our belief that splenorenal shunt is in general a less desirable procedure.

II. *Optimal time for surgery*

1. Patients with depressed liver function should be operated upon as soon as maximum improvement is reached following a vigorous medical regime; this should include the administration of human serum albumin in selected cases. If the medical regime is carried too long, the opportunity for surgery may be lost.
    a. Exsanguinating hemorrhage may intervene.
    b. Fatal cerebral involvement may occur.
    c. Prothrombin values may begin to fall after obtaining a maximum level.
    d. Serum protein values and albumin-globulin ratios may decline after reaching their peak.

2. Patients with fairly good liver function evidencing severe hematemesis should be operated upon as soon as possible following restoration of blood loss.

III. *Prognosis*

1. Patients surviving surgery can be assured relief from the effects of portal hypertension.[*]
    a. Esophageal varicosities eventually disappear, both clinically and by barium study.
    b. Congestive splenomegaly and hypersplenism resolve.
    c. Ascites and edema attributable to portal hypertension clear up; several weeks may elapse before improvement is noted.

2. Liver function studies may show no change, improvement, or slight regression.

IV. *The precautions to be taken and the pitfalls encountered in the performance of transthoracic portacaval shunt* may be summed up as follows:

1. The site for suture line should lie on the anterior or anteriomedial aspect of the inferior vena cava, in a plane lying between 90° and 180° relative to the right renal vein; the employment of a Satinsky clamp facilitates proper selection and control of the anastomosis site; a tilt table may be useful.

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[*] It is now two and one-half years since the first patient was operated upon. The spleen is nonpalpable and the patient has been completely free of symptoms; prior to surgery he had suffered a bout of hematemesis on the average of once every three months. The details of twelve additional cases will be reported upon in a subsequent paper.

2. Avoid angulation and/or tension of the suture line.

3. Care must be taken to place the transposed portal vein below an enlarged caudate lobe of liver. To accomplish this, resection of the caudal portion of the caudate lobe or anastomosis of the portal vein to the inferior vena cava below the level of the renal veins may be necessary.

4. Dissection of the portal vein is begun laterally so as to avoid injury to the common duct.

5. It is not necessary to shod the jaws of the Satinsky clamp. Shodding not only reduces available anastomosing space but interferes with accurate closure of the blades.

6. A portion of the inferior vena cava should be excised rather than simply incised.

7. Until completion of the anastomosis, a dilute heparin-saline solution should be employed locally to irrigate the intima of the inferior vena cava and portal vein.

8. Early ambulation is encouraged.

V. *The advantages of a transthoracic, thoracoabdominal portacaval shunt* are decisive and manifold and may be summed up as follows:

1. Exposure is excellent because of the free spread of the ribs, and the free communication of the chest and abdominal cavities.

2. The liver can be dislocated into the right hemithorax, since the restricting effect of the diaphragm is obviated. Access to the hilum of the liver is, therefore, direct and simple.

3. The structures in the lesser omentum are approached from the lateral aspect, advantageously presenting the portal vein to one side, instead of behind the common duct and hepatic artery.

4. Ligation of the right and left branches of the portal vein is possible. Such high ligation, flush with the liver, not only affords a longer segment of portal vein for anastomosis but offsets the chances of thrombus formation initiating in a blind venous pouch.

5. The inferior vena cava and the hilum of the liver are presented more superficially in the lateral than in the prone position.

6. Troublesome venous collateral circulation is more easily coped with by this direct exposure. Indeed, it is practically avoided, particularly the network within the hepatoduodenal ligament; these collaterals are often mistaken for "cavernomatous transformation of the portal vein," and frequently mislead the surgeon into abandoning attempts to establish a portacaval shunt.

7. By employing the thoracoabdominal route, portacaval shunts will be favored over splenorenal anastomosis. This is desirable for the following reasons:

    a. Portacaval shunt is more efficient.
    b. The function of the spleen is preserved.
    c. Failure to establish a portal-systemic anastomosis because of insurmountable perisplenitis is avoided.

d. Heparin is not required postoperatively as it is with splenorenal shunt. The large shunt and wide pressure gradients afforded by portacaval anastomosis, together with the precaution of excising *a portion of the inferior vena cava insure against spontaneous* closure of, or thrombosis at the suture line.

8. With the patient lying on the left side the suture line supports its maximum tension. The dependability of the suture line is, therefore, visualized immediately at the time of operation.

9. Because of the simpler technique of the thoracoabdominal approach, operative time is reduced by more than one-half, thereby avoiding the surgical shock associated with lengthy procedures and prolonged anesthesia.

10. The thoracoabdominal approach permits portacaval anastomosis to be carried out with minimum handling of intestine, thereby preventing or reducing considerably postoperative ileus.

11. Adhesions from a previous abdominal laparotomy or Talma-Morison operation are avoided. Moreover, there is less likelihood for the formation of anterior abdominal wall adhesions, with their attending complications.

12. The thoracoabdominal approach is less likely to give rise to incisional hernia, since the abdominal portion of the wound comprises a small part of the entire incision.

CONCLUSION

Thoracoabdominal approach for portacaval anastomosis appears to be the method of choice for the treatment of portal hypertension secondary to intrahepatic block. By means of this simplified approach, it is felt that portacaval shunt will achieve a more dynamic role in the therapy of portal hypertension.

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DISTURBANCES IN ACID-BASE BALANCE DURING ETHER ANESTHESIA

With Special Reference to the Changes Occurring During Thoracic Surgery

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CONSIDERABLE interest has been directed lately to the disturbances in acid-base balance of the blood occurring as a result of ether anesthesia during intrathoracic procedures. Beecher and associates[1] demonstrated the development of a progressive respiratory acidosis in the course of lobectomies and pneumonectomies. This acidosis was frequently uncompensated in that a definite, and sometimes ominous, fall in arterial plasma pH was encountered. In a number of instances the respiratory acidosis was complicated by the accumulation of fixed acids and therefore some degree of metabolic acidosis was also present.

The mechanisms by which carbon dioxide is allowed to accumulate in the alveolar air during anesthesia are not entirely clear. It was in an effort to elucidate these mechanisms that the present study was undertaken. It is self-evident that only by a clear understanding of the nature of the abnormalities in gas exchange can appropriate measures be taken to prevent this undesirable aspect of anesthesia.

MATERIAL AND METHODS

All patients studied were premedicated with barbiturates followed by morphine or demerol and atropine. Induction of anesthesia was accomplished by means of sodium pentothal and nitrous oxide. The latter was discontinued as soon as unconsciousness was reached, after which a mixture of ether and oxygen was given during the remainder of the operation. Closed intratracheal anesthesia was used in all cases except in kidney operations in which the ether-oxygen mixture was administered by means of a mask, using a closed system.

Six different groups of patients were studied. Five of these, namely, pneumonectomies, lobectomies, esophagectomies, thoracoplasties and kidney operations, were performed with the patients in the lateral position. The sixth group consisted of general surgical procedures on patients lying in the supine position.

Arterial blood, both for control studies and for observations during anesthesia, was collected under anaerobic conditions. One anesthesia sample was withdrawn as late as possible before anesthesia was discontinued. If the operation lasted for more than one hour, two or more blood samples were usually

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collected. The blood was taken to the laboratory where its analysis was immediately begun. Oxygen content of whole blood and CO_2 content of anaerobically separated plasma were determined in the Van Slyke manometric apparatus. Since the blood collected during anesthesia contained ether, the usual gasometric procedures could not be used. Oxygen content of this blood was determined by the method of Shaw and Downing,[5] while plasma CO_2 was analyzed by the Austin technique.[1] Duplicate determinations of the former checked within 0.1 volumes per cent, of the latter within 0.15 m. mol per liter. The oxygen capacity was determined by analysis of the blood equilibrated with room air in a flask for 20 minutes. In the presence of ether the air in the flask was flushed out repeatedly with a moist stream of room air before equilibration was started. The analysis could then be carried out in the routine fashion.[4] The plasma pH was measured in duplicate by means of the Van Slyke and associates photometric application to the Hastings-Sendroy technique.[7] The Beckman spectrophotometer, Model B, was used. The hematocrit value was calculated from the oxygen capacity.[4] The plasma pCO_2 and blood buffer base were found with the aid of the nomogram of Singer and Hastings.[6]

RESULTS

The results are tabulated in Tables I through VI. They can be summarized as follows:

1. In the great majority of cases in all six groups, a total of 48, a fall in arterial pH and a rise in arterial CO_2 tension were observed in each of the

TABLE I. SIX PNEUMONECTOMIES (INTRATRACHEAL ETHER-OXYGEN)

PATIENT	DIAGNOSIS	TIME AFTER POSITION (HOURS)	TIME PLEURA OPEN	O_2 SATURATION (%)	PL. CO_2 (M.MOL./L)	PL. pH	PCO_2 (MM. HG)	B.B.B. (MEQ./L)
Po	Tbc	:0	:0	87.52	26.93	7.46	37	50
		:10	:0	100.0	23.62	7.08	70	37
		:40	:20	100.0	18.06	7.38	30	41
		1:10	:50	100.0	21.06	7.32	39	41
Bu	Ca	:0	:0	94.15	24.83	7.32	46	44
		:20	:0	94.60	25.78	7.25	55	44
		2:30	1:45	85.60	34.65	6.82	170 ±	36
		(operation—just over on back-breathing O_2)		100.0	24.85	7.18	62	41
Fu	Ca	:0	:0	89.44	25.60	7.43	37	47.5
		:45	:20	95.88	22.91	7.33	41.5	43.5
		1:10	:45	99.89	22.95	7.32	42	43
Mu	Ca	:0	:0	92.04	19.25	7.33	35	40
		1:23	1:00	96.60	21.22	7.13	60	37
		1:40	1:17	90.75	21.07	7.19	52	38
Co	Tbc	:0	:0	94.07	23.79	7.44	34	46
		2:00	1:20	90.58	24.15	7.33	44	44
		3:30	2:50	87.43	25.57	7.32	48	45
St	Tbc (post thoracoplasty)	:0	:0	91.96	29.09	7.47	39	52
		1:25	:55	91.19	30.91	7.27	65.5	49
		2:20	1:50	94.91	28.88	7.31	54	48
		3:35	3:05	89.41	28.70	7.33	52	48

TABLE II. SEVEN LOBECTOMIES (INTRATRACHEAL ETHER-OXYGEN)

PATIENT	DIAGNOSIS	TIME AFTER POSITION (HOURS)	TIME PLEURA OPEN	O_2 SATURATION (%)	PL. CO_2 (M.MOL./L)	PL. pH	PCO_2 (MM. HG)	B.B.B. (MEQ./L)
Wa	Ca	:0	:0	93.58	26.20	7.43	38	49
		:10	:0	100.0	29.62	7.25	63	46
		1:50	1:15	99.70	35.52	7.04	120	44
Se	Hamartoma	:0	:0	97.95	23.69	7.42	35	45
		:31	:06	97.81	27.58	7.29	55	46
		1:35	1:10	100.0	27.71	7.23	61.5	44
Lo	Tbc	:0	:0	93.49	27.85	7.44	39.5	49.8
		1:00	:35	100.0	28.77	7.25	62	45.5
Ma	Tbc	:0	:0	91.61	22.60	7.45	32	44
		1:30	1:05	87.69	25.79	7.23	58	43
		3:45	3:20	90.55	26.52	7.25	57	44
Le	Bronchiectasis	:0	:0	89.78	28.90	7.46	39.5	51
		1:25	1:05	93.73	33.75	7.23	75	49
Ch	Blastomycosis	:0	:0	94.99	24.08	7.47	32	47.5
		1:25	1:15	100.0	23.27	7.27	48	41
Bu	Cystic disease Bronchiectasis	:0	:0	87.72	28.61	7.40	44	50
		1:30	1:12	100.0	39.28	6.96	170	43

samples withdrawn during anesthesia as compared with the control sample. In all but 7 of the 68 observations made during anesthesia, the arterial oxygen saturation was within normal limits.

2. All pneumonectomies (6 cases) and lobectomies (7 cases) showed this disturbance in acid-base balance. No significant differences were evident between the two groups. The greatest fall in pH encountered in each patient amounted to .11 and .39 units, except in one patient on whom a pneumonectomy was performed. This patient, a 50-year-old man (Bu) whose blood showed a fall in pH of 0.50 units, had had severe bleeding from the pulmonary artery just before the sample was taken. It is of interest that as long as 24 hours after the operation the pH was still 7.25. It had returned to normal on the third postoperative day.

The rise in arterial pCO_2 in the two groups under consideration amounted to 5 to 35.5 mm. Hg, except in Bu whose carbon dioxide tension mounted to 170 mm. Hg.

TABLE III. THREE ESOPHAGECTOMIES (INTRATRACHEAL ETHER-OXYGEN)

PATIENT	DIAGNOSIS	TIME AFTER POSITION (HOURS)	TIME PLEURA OPEN	O_2 SATURATION (%)	PL. CO_2 (M.MOL./L)	PL. pH	PCO_2 (MM. HG)	B.B.B. (MEQ./L)
Ow	Esophagitis	:0	:0	91.01	25.53	7.47	34	48
		1:08	:33	93.34	24.96	7.42	37	47
		4:10	3:35	88.02	25.94	7.42	38	49
Du	Ca	:08	:0	100.0	30.76	7.45	44	53
		1:50	1:25	96.94	30.95	7.42	47	52
				100.0	28.69	7.40	44	50
Hu	Ca	:0	:0	88.81	30.94	7.44	44	53
		2:55	2:20	100.0	27.58	7.31	52	47
		3:05	2:30	100.0	26.74	7.28	54	45

TABLE IV. THIRTEEN THORACOPLASTIES (INTRATRACHEAL ETHER-OXYGEN)

PATIENT	STAGE	TIME AFTER POSITION (HOURS)	O_2 SATURATION (%)	PL. CO_2 (M.MOL./L)	PL. pH	PCO_2 (MM. HG)	B.B.B. (MEQ./L)
Ge	1st (3 ribs)	:0	94.60	24.49	7.40	38	46
		1:00	100.0	22.45	7.37	37.5	---
Ma	2nd (3 ribs)	:0	94.77	28.54	7.42	42.5	50
		1:10	----	----	7.37	---	---
Ge	2nd (3 ribs)	:0	93.18	26.71	7.45	37	49
		:45	96.38	23.81	7.40	36.5	45
Po	Post pneumonectomy (4 ribs)	:0	93.28	27.99	7.51	34.3	51.5
		:28	100.0	26.26	7.40	41	47.5
Ha	2nd (3 ribs)	:0	91.43	26.90	7.35	46	47
		:43	100.0	24.66	7.28	47	44
Ma	3rd (4 ribs)	:0	87.01	28.14	7.41	43	49.5
		:33	100.0	27.17	7.35	47.5	46
Mo	1st (3 ribs)	:0	93.37	26.00	7.45	36	49
		1:18	100.0	22.73	7.44	32.3	46
		1:45	100.0	22.43	7.45	31.5	46
Du	1st (3 ribs)	:0	92.59	23.38	7.44	33.5	46
		1:10	100.0	23.08	7.30	44.5	43
Cl	1st (3 ribs)	:0	82.90	27.63	7.50	34.5	51
		1:20	83.77	28.11	7.32	52	47
Ta	1st (3 ribs)	:0	90.10	29.72	7.51	36	53
		1:40	100.0	24.92	7.47	32	48
Fi	1st (3 ribs)	:0	93.12	24.76	7.40	38.5	46
		1:30	94.12	22.98	7.35	40	44
As	1st (3 ribs)	:0	92.54	24.05	7.46	32.5	47
		1:25	100.0	26.91	7.40	41.5	47
Be	2nd (3 ribs)	:0	92.60	25.73	7.42	38	48
		1:00	100.0	22.26	7.36	38	44

TABLE V. EIGHT KIDNEY OPERATIONS (MASK ETHER-OXYGEN, CLOSED)

PATIENT	OPERATION	DIAGNOSIS	TIME AFTER POSITION (HOURS)	O_2 SATURATION (%)	PL. CO_2 (M.MOL./L)	PL. pH	PCO_2 (MM. HG)	B.B.B. (MEQ./L)
Mi	Left nephrectomy	Ca	:0	93.80	25.88	7.49	33	48
			:40	100.0	27.30	7.36	46	47
Ly	Left nephrectomy	Ca	:0	88.46	26.32	7.35	45	49
			:35	93.46	24.37	7.33	44	45
Su	Left nephrectomy	Pyelonephritis	:0	96.96	24.28	7.32	45	44
			1:05	100.0	23.46	7.23	53	40
Go	Right ureterostomy	Hydronephrosis	:0	91.50	31.33	7.43	47.5	51
			1:05	100.0	30.66	7.55	35	52
Ja	Removal left staghorn calculus	Kidney stones	:0	91.56	26.33	7.44	37.5	48
			1:00	100.0	27.99	7.27	57	45
St*	Removal tumor	Adrenal tumor	:0	89.36	28.11	7.49	36	50
			1:15	94.70	26.61	7.34	47	45
Br	Pyelolithotomy	Kidney stone	:0	91.77	24.98	7.42	37	47
			1:00	96.43	23.11	7.35	40	44
Ti	Right nephrectomy	Pyelonephritis	:0	91.34	23.47	7.42	35	45
			1:00	100.0	24.30	7.33	44	43

*Intubation in middle of operation.

TABLE VI. ELEVEN OPERATIONS ON BACK (INTRATRACHEAL ETHER-OXYGEN)

PATIENT	OPERATION	DIAGNOSIS	TIME AFTER INTUBATION (HOURS)	O_2 SATURATION (%)	PL. CO_2 (M.MOL./L)	PL. pH	pCO_2 (MM. HG)	B.B.B. (MEQ./L)
Bo	Craniotomy	Brain tumor	:0	93.30	26.01	7.49	34	50
			1:35	100.0	23.88	7.50	30	48
			3:00	100.0	23.57	7.45	33	47
Le	Subtotal gastrectomy	Ulcer	:0	94.06	24.35	7.43	35	46
			1:15	98.72	24.70	7.32	40	43.5
			2:40	100.0	20.85	7.33	38	41
El	Subtotal gastrectomy	Ulcer	:0	92.79	23.00	7.47	31	47
			2:00	97.69	24.77	7.33	44.5	45
			3:00	100.0	26.18	7.25	50.5	44
Gr	Subtotal thyroidectomy	Nontoxic goiter	:0	93.24	25.03	7.40	32	48
			1:30	100.0	23.19	7.34	41	44
Ro	Cholecystectomy	Gallbladder disease	:0	92.01	22.96	7.50	29	47
			1:25	----	22.27	7.38	36	--
Si	Subtotal thyroidectomy	Ca thyroid	:0	91.14	26.87	7.47	35.5	49
			1:00	100.0	25.80	7.39	41	46
Wi	Subtotal gastrectomy	Ulcer	:0	92.25	20.55	7.48	27	45
			2:20	100.0	32.32	7.05	108	42
Sh	Abdominoperineal resection	Ca rectum	:0	92.26	24.29	7.46	33	48
			1:20	96.34	27.23	7.31	51	47
			2:20	99.12	28.06	7.28	56	47
Fa	Right colostomy		:0	91.32	22.40	7.35	39	43
			:40	89.93	22.26	7.25	48	41
Po	Subtotal gastrectomy	Peptic ulcer	:0	96.43	29.02	7.42	43	52
			1:40	100.0	27.29	7.30	52.5	47
			2:15	----	28.16	7.22	64	45
Is	Abdominoperineal resection	Ca rectum	:0	95.12	25.08	7.44	36	46
			1:00	----	21.95	7.35	38	--
			2:05	100.0	26.06	7.22	61	42

Consistent evidence of the presence of a moderate degree of metabolic acidosis was found in the fact that the whole blood buffer base in all cases decreased to a maximum of 1 to 13 meq. per liter.

In those cases in which more than one blood sample was examined during anesthesia the changes in pH and pCO_2 were not always found to be progressive.

3. In three esophagectomies there was a maximal fall in pH of .05 to .21 units accompanied by a rise in pCO_2 of only 4 to 10 mm. Hg. These cases were under anesthesia for 2 to 4 hours, but better ventilation was maintained in them than in the lung resection cases.

4. The thoracoplasties (13 cases) and kidney operations (8 cases) can be considered together, as similar responses were encountered in the two groups. The *arterial* pH in these extrapleural procedures, carried out in the lateral position, fell to .01 to .17 units below the control observations. The arterial pCO_2 rose 1 to 19.5 mm. Hg in all but six instances in which a slight fall was observed. The blood buffer base fell 0 to 5 meq. per liter.

5. The blood findings were followed in 11 cases on whom general surgical procedures lasting from 40 minutes to 3 hours were performed. In 10 patients

the pH reached a level of .08 to .22 units below its control value; pCO_2 increased to 3 to 23 mm. Hg in excess of the preanesthesia level. One patient, a 53-year-old man with peptic ulcer, underwent a subtotal gastric resection in the course of which the pH fell to 7.05 and the pCO_2 mounted to 108 mm. Hg. This was the only observation made on this patient during anesthesia. The abnormalities were associated with a fall in systemic blood pressure.

The blood buffer base fell to 1 to 5 meq. per liter below its control value.

DISCUSSION AND CONCLUSIONS

The nature of the fixed acids which must have been released into the blood stream in each case of ether-oxygen anesthesia remains to be determined. The amounts of these acids were not greatly different in intrapleural procedures (average 4.7 meq. per liter) and in the remaining three groups of operations (average 3.0 meq. per liter). A consistent, though smaller, metabolic acidosis was also found by Beecher[2] in nonintrapleural procedures. On the other hand, his pneumonectomies and lobectomies showed nearly twice the degree of fixed acid accumulation found by us.

A degree of respiratory acidosis, as indicated by rising arterial CO_2 tension and falling pH, was present in most patients of each of the six groups. This was much more marked in the pneumonectomies and lobectomies. The most probable chain of events leading to the excessive increase in CO_2 tension of the alveolar air, and therefore of the arterial blood, is the following:

The respiratory center is primarily depressed by ether. This results in diminished alveolar ventilation with associated accumulation of CO_2. Far from having a stimulating effect upon the respiratory center, this increase in alveolar, and therefore arterial, pCO_2 further depresses a center already narcotized by ether. More impairment of ventilation follows; a vicious circle is thus set up leading to progressive accumulation of CO_2 in the alveolar air. That this chain of events does occur is confirmed by the observation that in none of the patients was an increase in ventilation observed during the course of anesthesia; on the contrary, the volume of ventilation seemed to be diminished in most instances.

It is therefore imperative that ventilation be *continuously* aided by extraneous means. This can consist of gentle and rhythmic manual kneading of the anesthesia bag or by any mechanical device which renders the same service. Failure to do this will be more harmful in pulmonary procedures than in extrapleural ones. The deflated state of the exposed lung, with maintenance of some blood flow through it, leads per se to accumulation of CO_2 in the arterial blood. However, it should be clear that keeping the lungs inflated is in itself not enough to permit adequate gas exchange.

The fact that in a number of patients some improvement in acid-base balance was observed as the operation progressed must be due to more effective kneading of the anesthesia bag, thereby leading to a temporary fall in alveolar pCO_2.

As the gas mixture administered contained more than 90 per cent oxygen, deficiency in arterial oxygen saturation should not be anticipated, even though alveolar ventilation is inadequate. It must be emphasized that no cyanosis is therefore expected under those conditions.

Brief mention should be made of other possible mechanisms leading to CO_2 accumulation. The intratracheal catheter itself does not increase the dead space. In the absence of extraneous assistance to ventilation the "pendelluft" (air moving from the operated lung into the healthy one and vice versa) might result in an increase of physiologic dead space, but this effect is probably small. The lateral position in which the patient is placed in all intrapleural operations studied in this series has been suspected by Beecher of leading to respiratory acidosis.[3] Comparison of our results in thoracoplasties and kidney operations with those in operative procedures carried out with the patient in the supine position, fails to substantiate this possibility.

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CONTINUOUS SPINAL ANESTHESIA FOR THORACOPLASTY

SECOND REPORT

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IN 1947, one of us (G. W.),[1] reported a series of 300 thoracoplastic operations performed under continuous spinal anesthesia. These cases were operated upon from February, 1941, to December, 1944. In the ensuing four-year period, the same anesthesia was used for all thoracoplasty operations. In view of the fact that it has continued to be satisfactory for both patient and surgeon, we believe it warrants another report.

Induction of continuous spinal anesthesia was attempted in 574 thoracoplasty operations during the four-year period ending December, 1948. These operations were done on 219 patients suffering from pulmonary tuberculosis. There were 115, or 52 per cent, male patients and 104, or 48 per cent, female patients, ranging in age from 17 to 60 years, with more than 60 per cent being under 40 years of age.

As an aid to comparative study, the cases have been divided into three groups: (1) unilateral pulmonary tuberculosis, 195 cases; (2) bilateral pulmonary tuberculosis, 237 cases; and, (3) bilateral pulmonary tuberculosis with contralateral pneumothorax, 142 cases. In addition to a stage of thoracoplasty, 87 patients had a Semb extrafascial apicolysis performed.

TECHNIQUE

The technique, as described in the first report, has remained essentially the same and only the salient steps will be repeated.

The patient is placed on the table in the position to be maintained during operation and should be moved as little as possible. Ephedrine sulfate, ⅜ grain, is given hypodermically and a skin wheal is raised in the lumbar region over the widest palpable interspace. A No. 19 gauge malleable spinal needle is used. If a free flow of spinal fluid is not obtaind, or if the fluid is bloody, a second puncture is made at another interspace. If either of these conditions still prevails, the operation is postponed. *A free flow of clear spinal fluid is absolutely essential.* Twenty cubic centimeters of spinal fluid is slowly withdrawn and is used to dissolve 500 mg. of procaine—2½ per cent solution. The needle is bent to the desired position and connected with the flexible rubber tubing. The tubing is then fixed to the patient's skin with adhesive tape. The operating table is lowered 10 to 15° at the head.

An initial dose of 100 mg. is administered and subsequent 50 mg. doses of procaine are given at two-minute intervals until the desired level of anesthesia is reached. It is rarely necessary in a first-stage thoracoplasty to give more procaine after the level of anesthesia has reached the mid-portion of the scapula. While the patient is prepared and draped, the anesthesia level will rise to the angle of the jaw. After closure of the muscle layers, the stopcock on the tubing is opened and spinal fluid withdrawn in the amount given as an anesthetic solution. This hastens the return of motor and sensory functions so that by the time the skin incision is closed and dressings are applied, our patient is able to move the lower extremities and has return of tone to the abdominal muscles. The spinal needle is not

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withdrawn until the level of sensation is at the lower angle of the scapula and the abdominal muscle tone or the ability to move the lower extremities is present.

The thoracoplasty patient, who has been anesthetized with continuous spinal anesthesia and has this degree of return of function, does not go into shock, remains cooperative, and is *able to cough up secretions without difficulty. The postoperative nursing care, which is* very difficult to obtain in sanatoriums, is greatly simplified.

Oxygen is given by mask to all patients as soon as the operation is begun and whole blood is transfused during this procedure as in any other major operation.

DOSAGE

The initial dose is usually 100 mg. of procaine and is followed with supplemental doses of 50 mg. at two- to three-minute intervals until the desired level is reached (the angle of the jaw for a first-stage thoracoplasty). Occasionally, subsequent doses must be given during the operation to maintain the desired level of anesthesia. The total dosage in this series has varied from 150 mg. to 2,200 mg. of procaine. However, 65 per cent of the stages have been done with a total dosage of procaine ranging from 150 mg. to 500 mg.

A 2½ per cent solution of procaine has proved to be the most satisfactory from the standpoint of a reasonably prompt induction as well as the matter of safety. The safety *factors mean the observation of at least a two-minute interval before administering an ad*ditional amount of drug. In this series, 5 cases, or 0.8 per cent, had respiratory distress which could be attributed, at least in part, to the anesthetic. All responded promptly to withdrawal of the drug, positive pressure oxygen, and artificial respiration to aid the removal of the carbon dioxide.

EFFECT ON PULSE, BLOOD PRESSURE, AND RESPIRATION

An analysis of the statistics sumarized in Table I reveals no appreciable difference in the effect of spinal procaine on the pulse rate, blood pressure, or respiration of the three groups of patients studied. A diminution in pulse rate averaging 14 per minute was shown by 13.8 per cent of cases in Group 1 at the conclusion of operation. In Group 2, 16 per cent showed a fall averaging 17 per minute and 12 per cent of cases in Group 3 showed a fall averaging 19 per minute. A rise in pulse rate averaging 19 per minute was shown by 14.1 per cent in Group 1. In Group 2, 17.6 per cent of cases showed a rise averaging 19 per minute and 9½ per cent of the cases in Group 3 showed a

TABLE I

	PULSE				BLOOD PRESSURE				RESPIRATIONS				OPERATIONS DISCONTINUED
GROUP	FALL	RISE	NO CHANGE	NO RECORD	FALL	RISE	NO CHANGE	NO RECORD	FALL	RISE	NO CHANGE	NO RECORD	
1. Unilateral 100 cases (33%)	79	81	25	5	114	11	8	57	18	110	28	84	5
Percentage	13.8	14.1	4.3	0.8	19.8	1.9	1.4	9.9	3.1	19.2	4.8	5.9	0.8
2. Bilateral 224 cases (39%)	92	101	29	2	152	14	7	51	24	134	88	28	13
Percentage	16	17.6	5	0.3	26.5	2.4	1.2	8.8	4.2	23.4	6.6	4.8	2.2
3. Bilateral with pneumothorax 136 cases (24%)	70	55	9	2	87	11	5	33	8	96	26	6	6
Percentage	12	9.5	1.6	0.3	15.1	1.9	0.8	5.8	1.4	16.7	4.5	1	1

rise averaging 18 per minute. No change in pulse rate was recorded in 4.3 per cent of cases in Group 1, 5 per cent of Group 2, and 1.6 per cent of Group 3. There was incomplete data in 9 cases.

Complete records pertaining to blood pressure were available in 133 cases of Group 1, 173 cases of Group 2, and 103 cases of Group 3. A decrease in blood pressure was shown by 19.8 per cent of these cases in Group 1 at the conclusion of operation. In Group 2, 26½ per cent showed a fall and in Group 3, 15.1 per cent showed a fall. A rise in blood pressure was noted in 1.9 per cent of these cases in Group 1. In Group 2, 2.4 per cent and in Group 3, 1.9 per cent showed a rise in blood pressure at the conclusion of operation. No change in blood pressure was recorded in 1.4 per cent of cases in Group 1, 1.2 per cent of Group 2, and 0.8 per cent of Group 3.

Thirteen patients, or 2.2 per cent, went into a shocklike state during continous spinal anesthesia. The degree of shock was determined entirely by a markedly diminished blood pressure and an elevated pulse. However, the skin remained warm and dry in every instance. All responded promptly to withdrawal of the drug and transfusion of whole blood.

Complete data pertaining to respiration were recorded in 156 cases of Group 1, 196 cases of Group 2, and 130 cases of Group 3. A fall in respiration averaging 5 per minute was noted in 3.1 per cent of these cases in Group 1. In Group 2, 4.2 per cent showed a fall averaging 4 per minute and 1.4 per cent of cases of Group 3 showed a fall averaging 4 per minute. A rise in respiratory rate averaging 6 per minute was noted in 19.2 per cent of cases in Group 1. In Group 2, 23.4 per cent showed a rise averaging 7 per minute and 16.7 per cent of cases in Group 3 showed a rise averaging 8 per minute. No change in respiratory rate was noted in 4.8 per cent of cases in Group 1, 6.6 per cent of Group 2, and 4.5 per cent of Group 3.

COMPLICATIONS

There was no appreciable difference in the incidence of complications in the three groups of patients studied. During the operative procedure, 18 per cent of the patients complained of nausea and 2 per cent of vomiting or retching. All but 3 patients, or 0.5 per cent, were immediately relieved by withdrawal of spinal fluid usually 2 to 4 c.c. in amount.

In the previous report,[1] 4⅓ per cent of our patients complained of nausea and 13 per cent had vomiting. We believe the reversal of figures can probably be attributed to the fact that we now recognize the symptoms earlier and also to the use of a more dilute solution.

Postoperative headache occurred in 32 cases or 5.7 per cent. In none of these was the headache severe and in only one was it persistent, lasting for one week. Postanesthetic urinary retention, though of short duration, occurred in 2 patients, requiring catheterization.

Two patients developed a myeloradiculitis postoperatively. The first patient had a lower motor neurone paralysis on the right side with a level at the ninth thoracic dermatomere. She showed gradual improvement during the postoperative course but on a follow-up visit one year later, there was still evidence of a partial paralysis of the right leg. The second patient showed evidence of a complete transverse lesion of the spinal cord at the level of the twelfth thoracic dermatomere. This occurred approximately twenty-four hours postoperatively. There was some improvement during the immediate postoperative period as evidenced by a return of sensation in the first, second, and third lumbar dermatomeres. One month following operation, this patient died of a pulmonary embolus.

In the preceding case, the paralysis occurred following the third stage of thoracoplasty under continuous spinal anesthesia and the operative procedure in each instance, as well as the anesthetic, was uneventful. The patient was able to move the lower extremities at the conclusion of each stage. The time interval between stages was three weeks. At the first stage, 750 mg. of procaine were used, at the second, 450 mg. and at the third, 900 mg. of procaine had been administered. This is an unusually large dose for a third-stage operation and there is no reason given in the record explaining this fact nor is there any time chart showing the intervals. It was noted that no bloody fluid was obtained. The free flow, however, was intermittent and lack of a constant free flow is an absolute contraindication to the administration of any spinal anesthetic. (We were subsequently informed that the patient had been under treatment for some years for syphilis, but this was not noted on the hospital record. Whether or not the syphilitic infection played a part in causing the myeloradiculitis is debatable.)

In 24 cases it was necessary to discontinue the operation because of difficulty with the induction of the anesthetic or unsatisfactory condition of the patient. These cases are listed as failures of this particular type of anesthesia, although, in some instances, other factors prevailed. These failures are briefly summarized in the following paragraphs.

CASE 1.—Unilateral pulmonary tuberculosis. Free flow of spinal fluid could not be obtained. Satisfactory level was not obtained after 700 mg. of procaine had been given. (No drug should have been given. Error in technique and judgment.)

CASE 2.—Unilateral pulmonary tuberculosis. Operation canceled because of bloody spinal tap. (Error in technique.)

CASE 3.—Unilateral pulmonary tuberculosis. Four taps were made but free flow of spinal fluid could not be obtained. (Error in technique.)

CASE 4.—Unilateral pulmonary tuberculosis. Spinal fluid bloody; 500 mg. of procaine given but no anesthesia obtained. (Error in technique and judgment.)

CASE 5.—Unilateral pulmonary tuberculosis. Three taps made but bloody fluid obtained each time. (Error in technique.)

CASE 6.—Bilateral pulmonary tuberculosis. Satisfactory level was not obtained after 480 mg. of procaine had been given. (No record as to free flow. Error in technique and judgment.)

CASE 7.—Bilateral pulmonary tuberculosis. Patient's blood pressure fell to 55/45 after 175 mg. of procaine had been given. (Patient in very poor general condition. Error in judgment.)

CASE 8.—Bilateral pulmonary tuberculosis. Patient received 900 mg. of procaine in first thirty minutes in order to obtain satisfactory level. Respirations became shallow and difficult. Pulse rose to 140 and blood pressure dropped to 60/50. (Excessive dosage in a short interval. Error in judgment.)

CASE 9.—Bilateral pulmonary tuberculosis. Satisfactory level could not be obtained. Later it was discovered that the patient received just a fraction of the dose it was thought he received, as new tubing contained 6 c.c. instead of the usual 2 c.c. (Error in technique.)

CASE 10.—Bilateral pulmonary tuberculosis. Patient had pain in left groin, leg, and foot following tap. No free flow of spinal fluid obtained. Satisfactory level not obtained after 300 mg. of procaine had been given. (This patient fortunately did not develop a myeloradiculitis. Error in technique and judgment.)

CASE 11.—Bilateral pulmonary tuberculosis. Marked paradoxical breathing developed after segment of rib removed and operation was discontinued. (No apparent error in technique or judgment.)

CASE 12.—Bilateral pulmonary tuberculosis. Pulse rose to 180, fifteen minutes after 150 mg. of procaine were given. Tachycardia persisted despite all effort to overcome it and surgery, therefore, was canceled. (Patient's pulse rate was 140 at the time of the induction of the anesthetic. Grave error in judgment.)

CASE 13.—Same patient as preceding one. Pulse rose to 192 after anesthetic was begun. Supplemental sodium pentothal analgesia was induced but tachycardia persisted and operation was canceled. (Error in judgment repeated.)

CASE 14.—Bilateral pulmonary tuberculosis. After 150 mg. of procaine had been given, pulse rose to 160 and blood pressure dropped to 80/65. Operation canceled. Patient promptly responded to withdrawal of drug, oxygen, and transfusion of whole blood. (Very poor risk. Error in judgment.)

CASE 15.—Bilateral pulmonary tuberculosis. Operation canceled because of bloody spinal taps. (Error in technique.)

CASE 16.—Bilateral pulmonary tuberculosis. After 250 mg. of procaine had been given and before surgery started pulse rose to 150 and respiratory rate to 36. Patient responded to transfusion of blood and withdrawal of drug. Operation canceled. (No note as to free flow. Error in technique and judgment.)

CASE 17.—Same patient as preceding one. Induction of anesthesia with a pulse rate of 120. After 200 mg. of procaine had been given and the skin and muscles had been incised, the pulse rate rose to 170 and blood pressure was recorded as 90/60. Operation immediately discontinued. (Error in judgment repeated.)

CASE 18.—Bilateral pulmonary tuberculosis. After 100 mg. of procaine had been given and before surgery was begun, the pulse rose to 165 and blood pressure dropped to 80/65. Operation immediately canceled. (No error in technique or judgment.)

CASE 19.—Bilateral pulmonary tuberculosis with contralateral pneumothorax. Patient had respiratory arrest following mobilization of scapula. Prompt recovery with oxygen, artificial respiration, and withdrawal of spinal fluid. (A total of 500 mg. of procaine had been given. However, without checking the anesthetic level again, supplementary doses were given after the desired level had been reached. Error in judgment.)

CASE 20.—Bilateral pulmonary tuberculosis with contralateral pneumothorax. Blood pressure dropped to 30 systolic after 400 mg. of procaine had been given. Prompt recovery with transfusion of whole blood, withdrawal of drug, and administration of oxygen under pressure. (Patient had an overdosage in a short time interval. Error in judgment.)

CASE 21.—Bilateral pulmonary tuberculosis with contralateral pneumothorax. After skin and muscle layers were incised, the pulse rate rose to 120 and blood pressure dropped to 80/60. Operation discontinued. (Error in judgment.)

CASE 22.—Bilateral pulmonary tuberculosis with contralateral pneumothorax. Patient had no anesthesia after 650 mg. of procaine had been given, although a good flow was present. Patient became very nervous and apprehensive and operation was canceled. (Very uncooperative. This case should never have been tried. Error in judgment.)

CASE 23.—Bilateral pulmonary tuberculosis with contralateral pneumothorax. It was impossible to get the anesthetic level above the eighth interspace. Operation completed under local anesthesia. (No note of free flow. Patient had a total dosage of 725 mg. of procaine. Error in technique and judgment.)

CASE 24.—Bilateral pulmonary tuberculosis with contralateral pneumothorax. After 150 mg. of procaine had been given and before surgery started, pulse rate rose to 160. Operation deferred. (No error.)

In summarizing the 24 failures, we note that 21, or 87½ per cent, are due to errors in technique or judgment or both and in only 3 cases could no error be detected. A large percentage of these failures occurred in the hands of the Junior Residents; hence, we wish to point out that with improvement in skill and judgment, failures will be minimal.

SUPPLEMENTARY ANESTHESIA

In this series it was necessary to use one or more supplementary anesthetic agents in 28 cases. These agents are listed in Table II.

TABLE II

	CASES
½% or 1% procaine by local infiltration	21
Nitrous oxide	2
Local infiltration and sodium pentothal	2
Cyclopropane	1
Cyclopropane and paravertebral block	1
Nitrous oxide and ether	1

The percentage of operations thus requiring supplemental anesthesia was 4.8: the effectiveness of continuous spinal anesthesia in this series being 95.2 per cent. When the 24 cases which were discontinued are added to this group, the total effectiveness of the continuous spinal anesthetic method is 91.2 per cent.

MORTALITY

There were 2 deaths in the operating room in this series which are briefly described in the following paragraphs.

The first patient was a 36-year-old woman with bilateral, far-advanced pulmonary tuberculosis with pneumothorax on the left side. Thoracoplasty was attempted on the right side. The anesthetic was administered without incident and the patient received 390 mg. of procaine during the one and one-half-hour operative procedure. The only ill effect noted was rather severe nausea, which was relieved by withdrawal of spinal fluid. During the operation, a traumatic pneumothorax was induced by a tear in the pleura. The intrapulmonic pressure was increased but the lung could not be completely re-expanded. The defect was then closed and air was aspirated, thus establishing a good negative pressure but the disturbed pulmonary function in this seriously ill patient could not be restored. The respirations became increasingly more shallow and finally ceased. No drug was withdrawn.

The second patient was a 28-year-old man with bilateral, advanced pulmonary tuberculosis with pneumothorax on the right and cavitation on the left side. The anesthetic was administered with difficulty. The patient received 550 mg. of procaine in thirty-four minutes. Severe paradoxical motion with poor pulmonary ventilation developed after portions of the second and third ribs were resected. The operation was immediately discontinued. Withdrawal of drug was begun, tracheal intubation was also done, and artificial respiration administered. The airway was clear and in spite of artificial respiration, cyanosis increased, respirations became more shallow and then ceased.

Both of these patients were very poor risks with reduced pulmonary function as a result of the extent of the disease on the operative side as well as the reduced function in the contralateral lung due to artificial pneumothorax. Both deaths should be classified as due to errors in technique and judgment. Both of these anesthetics were administered by Junior Residents.

ANALYSIS OF HEADACHES

The cause and management of postspinal headache have been a subject of much thought and investigation for many years.[2, 3, 4] The dosage of the anesthetic agent is thought to play no part in its production.[5] Such headache has been ascribed by a minority to increased intracranial pressure and by a majority to decreased intracranial pressure.[6] Some claim that faulty technique and the size of the needle are contributory factors.

As previously stated, 32 patients, or 5.7 per cent, developed postspinal headaches in this series. This is not a large number of patients nor should it mitigate in any way against the use of this type of anesthesia. Watson[7] quoted Waters as analyzing 40,000 cases of cyclopropane anesthesia and finding the incidence of postanesthetic headache to be 10 per cent.

A No. 19 gauge malleable spinal needle is used and is kept in situ from one to three hours. Our patients are immediately returned to bed following surgery and instructed to lie flat for six to eight hours.

In 29, or 90 per cent, of the patients with headache, the technique was excellent in that a single tap was made and a free flow of clear spinal fluid was obtained. In 3 cases, multiple punctures were necessary before the anesthetic could be started. Thus, it would seem that in this series faulty technique did not play much of a role in the production of headache. Spinal fluid pressures were recorded in 25 of the 32 cases of headache. In 5 cases, or 20 per cent, the spinal fluid pressures recorded at the end of the operation were increased above normal. In 8 cases, or 32 per cent, the final spinal fluid pressures were decreased below normal and in 12 cases, or 48 per cent, the final spinal fluid pressures were within the normal range. Faulty technique, the amount of drug used, and the change in spinal fluid pressure, therefore, seem to bear no significant relation to the incidence of postspinal anesthetic headache. The one common factor was the state of apprehension and anxiety during the preoperative period.

ADVANTAGES

The advantages of continuous spinal anesthesia for thoracoplasty are those of an anesthetic method that affords the patient maximum safety and comfort during the operation and minimal discomfort postoperatively. These patients are quiet, relaxed, and have even, steady respiratory excursions during the operative procedure. Anoxia, cyanosis, and paradoxical motion of the lung is at a minimum since the respiratory reserve of these chronically ill patients is not compromised by the added burden of an inhalation anesthesia. On return from the operating room, the patient is alert, can move about in bed, and is able to cough up secretions. Return to a full diet occurs usually the next day and is much more rapid than following a general anesthetic. There have been no postoperative pulmonary complications related to the anesthetic in any way in this series. The complete absence of the distressing postanesthetic prostration seen so frequently with inhalation anesthesia aids immeasurably in the prompt uneventful operative recovery of these patients.

CONCLUSIONS

1. Continuous spinal is the anesthetic method of choice for extrapleural thoracic procedures from the standpoint of patient safety and better surgical performance.
2. The technique is easily mastered and the effort expended is rewarded by a prompt operative recovery and a smoother postoperative course.
3. The complications occurring with this method are fewer than following inhalation anesthesia. They can be overcome in a great majority of cases by intelligent and skillful management.
4. Postoperative nursing requirements are reduced to a minimum.

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ACANTHOSIS NIGRICANS ASSOCIATED WITH CANCER OF THE LUNG

Report of a Case

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THE association between acanthosis nigricans and visceral carcinoma is too well known to require repetition. However, the rare occurrence of involvement of the respiratory tract by the malignant process seems sufficient reason to warrant reporting a case. Curth,[1] in 1943, reviewed the literature very thoroughly and found 384 reported cases of acanthosis nigricans of which 191 were associated with cancer of an internal organ and 193 were of the so-called benign type in which only the skin lesion was present. In the former group she found three cases of cancer of the lung and of these only two were proved by post-mortem examination. Of the 191 cases associated with cancer, the tumor was abdominal in 92.67 per cent while the breast was the site of the malignancy in 4.7 per cent. In one case mediastinal cancer was suspected but not proved. Curth's review gives a very complete bibliography of the literature up to 1943. Since that date there have been no additional cases reported of cancer of the lung in association with acanthosis nigricans.

CASE REPORT

H. D., a 50 year-old white man, was admitted to the Veterans Administration Hospital, Manhattan Beach, April 8, 1948, complaining of cough and expectoration and shortness of breath of four weeks' duration. He had a chronic cough during the past eighteen years and, during November, 1945, had had lobar pneumonia from which he never made a complete recovery. In March, 1948, he developed sharp pain across the anterior portion of the midchest, shortness of breath on exertion, increase in cough, especially at night. He developed a low-grade fever and was said to have fluid in the chest. Since February, 1948, he had noted that the skin in the axillae, nipples, and around the base of the neck had become increasingly dark. There had been a loss of forty pounds since February, 1948.

The family history was noncontributory. There were nine siblings, none of whom were known to have had skin changes or malignant disease. His father died of arteriosclerotic heart disease. His mother was living and well.

The past history revealed he had a skin lesion on the right side of the face for which he received injections of ''gold and liver'' in 1943. The nature of this lesion was not known.

Physical Examination.—On admission, temperature was 101.4° F., the pulse 104, the respirations 28, and the blood pressure 92/60. He was a well-developed and moderately nourished white man appearing chronically ill and in mild respiratory distress. Surrounding the

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nipples, in the axillae, at the base of the neck, particularly posteriorly, and between the digits of both hands, there were marked deposits of dark brown pigment. In the axillae and about the base of the neck, the skin was velvety in appearance with increase in thickness. The nasal septum was deflected to the right and the nasal mucosa was congested. There were many missing teeth and considerable caries of those remaining. From the angle of the right scapula to the base of the lung there was dullness to percussion with numerous medium moist râles but no change in breath sounds. There was no abnormality noted in the cardiovascular system. There were well-healed scars in the right inguinal region and the right lower quadrant at the sites of previous herniorrhaphy and appendectomy, respectively.

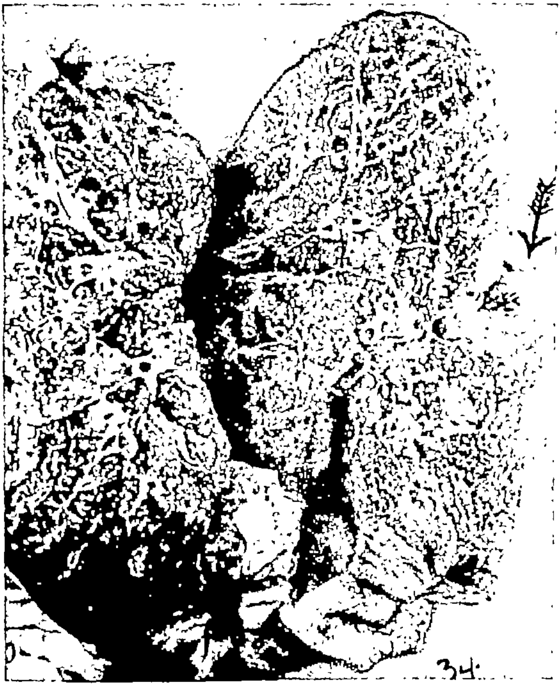

Fig. 1.—Right lung showing primary tumor mass and secondary infiltration.

Laboratory Findings.—The hemoglobin was 12.5 Gm., the red blood cell count 4,400,000, the white blood cell count 13,500, 83 per cent neutrophils, 12 per cent lymphocytes, 4 per cent monocytes, 1 per cent eosinophils, sedimentation rate 28 (Wintrobe); urinalysis negative; Kahn negative. Sputum was examined repeatedly for tubercle bacilli and none were found. Blood culture was negative. X-ray examination of the chest showed a thick-walled abscess, probably carcinomatous, at the apex of the right lower lobe. There was some pneumonic infiltration of the left lower lung and bilateral pleuritic infiltration adjacent to the left diaphragm. Electrocardiogram showed auricular fibrillation on one occasion and normal sinus rhythm on another and there were evidences of myocardial damage as well.

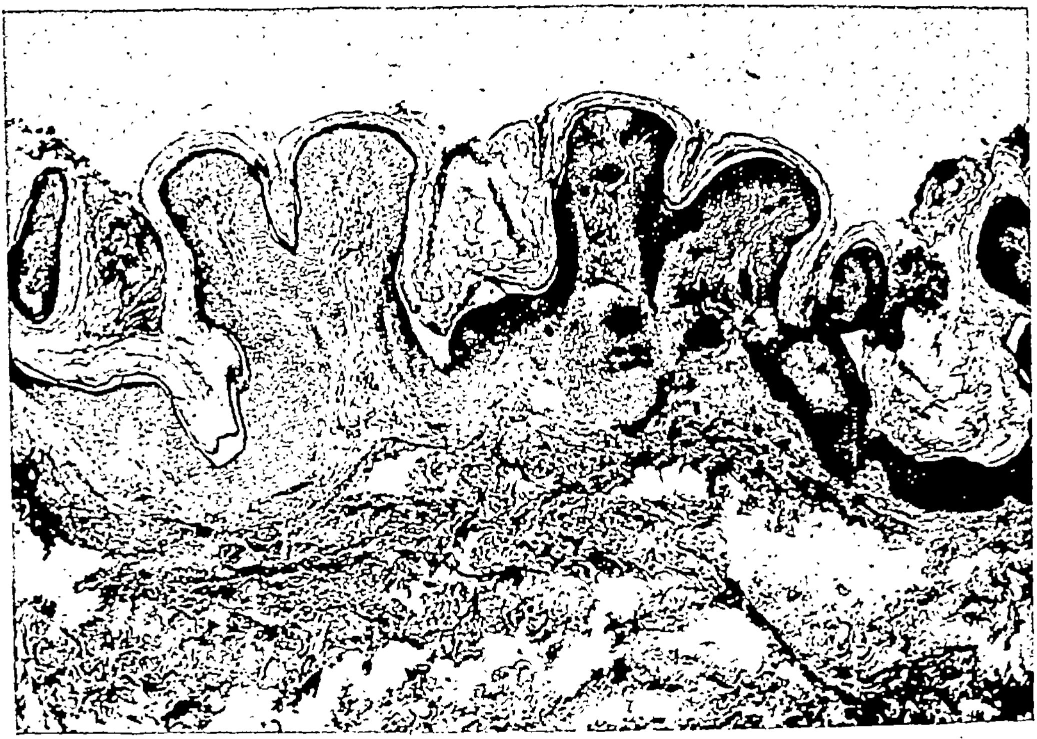

Fig. 2.—Low-power section of involved skin showing papillary hyperkeratosis and increase in prickle cell layer (acanthosis).

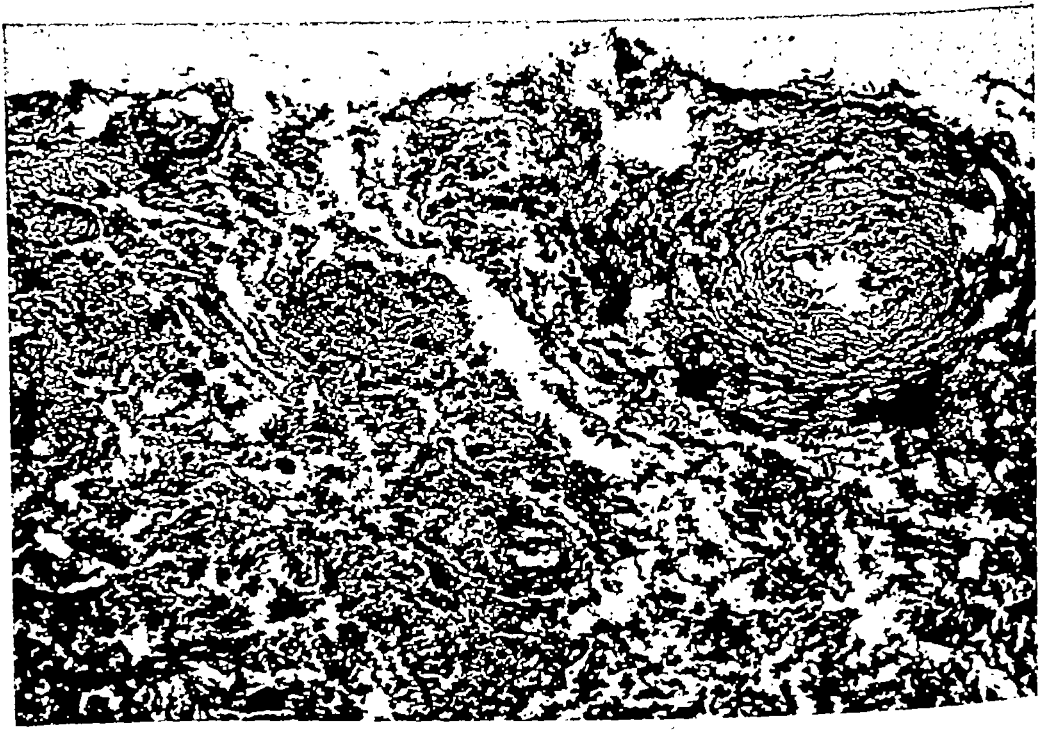

Fig. 3.—Low-power section (×80) of lung showing invasion by tumor tissue.

Course in Hospital.—During the period of hospitalization, he ran a septic temperature, ranging between 99° and 103° F. He reeived penicillin without effect. Bronchoscopy was done in an attempt to find the site of the tumor, but only large quantities of thick tenacious sputum were seen in the right bronchus. Dyspnea became progressively worse and in spite of supportive therapy, he died on April 26, 1948.

Post-mortem Examination.—Autopsy was performed* and the examination revealed fibrous adhesions in both pleural cavities with about 200 c.c. of slightly cloudy amber fluid. The pericardial sac was obliterated by fibrous adhesions. The lower lobe of the right lung was partially adherent to the pericardium, which in turn was adherent to the diaphragm. There were discrete, firm, lymph nodes in the superior mediastinum which were creamy white in color and cheesy in consistency. Many of the lymph nodes contained anthracotic pigment. The left lung was smaller than usual and boggy. On section, it was edematous and contained atelectatic and fibrotic areas. The bronchioles were dilated and the walls roughened and thickened. The lumen was filled with thick tenacious blood-tinged exudate. The right lung filled the entire pleural cavity and weighed 1,500 Gm. and was firm in consistency. On section, the upper lobe was firm and almost non-air-containing. The outer one-third of the superior portion of the lower lobe contained a more or less circumscribed grayish-white, friable, firm mass, 4 cm. in diameter with a central cavity 1 cm. in diameter which was filled with a thick green purulent exudate. No bronchiole could be traced in this area (Fig. 1). The remaining portion of the lower lobe was firm; friable, and contained purulent exudate. Careful dissection of the right bronchial tree failed to show any ulceration or tumor. Bronchial lymph nodes averaged 1 to 2 cm. in diameter and were firm in consistency. The heart weighed 300 grams. The pericardium was thickened and measured up to 0.5 cm. in some sections. There was no unusual thickening of the ventricular walls. The coronary arteries were all patent. The esopha-

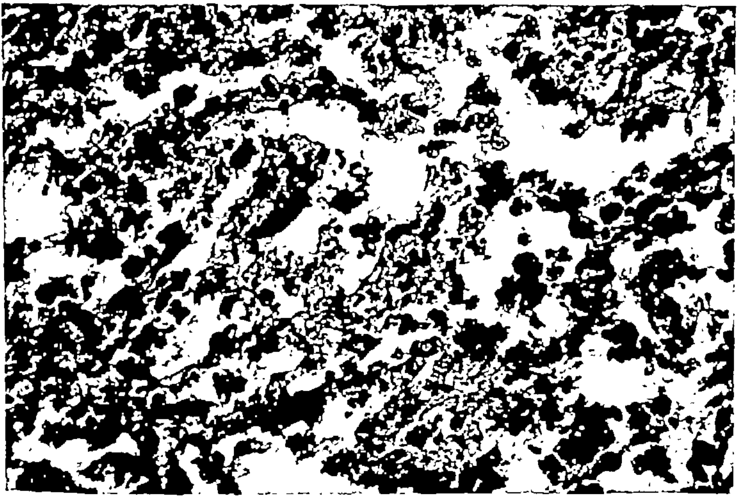

Fig. 4.—High power (×450) of same portion of lung showing anaplastic cancer cells with hyperchromatic nuclei.

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*By Dr. Lester M. Fox, Chief of Pathological Service at Veterans Administration Hospital, Manhattan Beach.

gus was surrounded by several 1 cm., fairly firm, lymph nodes of cheesy consistency. The mucosa of the esophagus, stomach, and small and large intestines was free of any ulceration or neoplasm. The kidneys were normal.

Microscopic Examination.—There was papillary hyperkeratosis of the skin and formation of epithelial papillae with long, thin, rete pegs. The prickle cell layer was moderately thickened. Some of the basal cells contained melanin (Fig. 2). The involved portion of lung showed marked distortion of the architecture, thickening of the pleura, and invasion by tumor cells. Lung tissue was invaded by masses of these cells which were large, round, polygonal, hyperchromatic, and in some areas, giant cell in type. The nuclei were large, almost filling the cell, and having only a small rim of cytoplasm. There was no definite grouping or distinguishing features. The interstitial tissue was also invaded by tumor cells following the aforementioned pattern. Many of the alveoli were filled with sheets of tumor cells, giving the appearance of a pneumonitis. The linings of lymph vessels were replaced by tumor cells and in many places the lumens and walls of the lymphatics were filled with tumor tissue. The adjacent alveoli were collapsed and hemorrhagic (Figs. 3 and 4). The lymph nodes showed distortion of architecture with complete invasion by hyperchromatic, bizarre-shaped, large, round, and polygonal cells, some of which were multinucleated. In some sections, the capsule of the gland was thickened and much of the tumor tissue was necrotic. There was marked thickening of the visceral pericardium with vascularization and fibrosis. Focal areas of round and plasma cells still persisted and there were nests of tumor cells, some of which were found in the lymphatics of the epicardium. There was no evidence of metastasis to other organs.

DISCUSSION

The significance of the association between a skin lesion in itself benign and cancer has been discussed recently by Curth,[2] who pointed out the various theories which have been propounded to explain this association. It was long thought that pressure from the cancerous lesions in the abdomen on the adrenals or the sympathetic chain was responsible for the pigmentary cutaneous changes. However, the occurrence of the small percentage of cases of extra-abdominal malignancy disproves this theory and, where tests for adrenal insufficiency have been carried out, they have been uniformly negative. Genetic relationships between acanthosis and cancer seem to exist. A study of the case reported here, however, reveals no familial history of similar disease, but the history of collaterals was not carefully investigated and, therefore, no real conclusions can be drawn.

The possible influence of steroid hormones[3] on the development of acanthosis has been suggested because of the appearance of the lesion with the onset of menstruation in at least two members in one family. In our case, no such influence was suggested either by the history or physical findings.

Whatever the fundamental reasons may be, it seems apparent that there must be a close etiological connection between the skin lesion and the visceral neoplasm. It is a curious and certainly provocative coincidence that a characteristic and unmistakable external lesion is in 50 per cent of the cases associated with an internal malignant tumor. Further studies are certainly needed to clarify this relationship and, perhaps, to give an answer to the problem of what initiates the cancerous growth in one group of cases but is lacking in the other. The internist or dermatologist who first sees and recognizes acanthosis nigricans has a responsibility to solve this perplexing riddle.

SUMMARY

A case of acanthosis nigricans occurring in a 50-year-old white man in association with anaplastic carcinoma of the lung is reported. This is the third proved case of carcinoma of the lung to be reported as occurring with acanthosis nigricans. The possible etiological factors are briefly discussed.

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A REPORT OF A CASE OF LOCALIZED BRONCHOPULMONARY ASPERGILLOSIS SUCCESSFULLY TREATED BY SURGERY

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BRONCHOPULMONARY aspergillosis was first described by Virchow in 1856. Toward the end of the nineteenth century the disease was reported with increased frequency among pigeon feeders and hair manipulators in France. The organism was present in the grain which the pigeon stuffers masticated and then fed directly into the mouths of the birds. In the case of the wig makers, corn meal was used to degrease the hair and the men frequently worked in an atmosphere heavy with its dust. It was thus considered a primary occupational disease, which was also known to occur among other grain handlers, such as threshers and fur cleaners who use rye flour for degreasing.[1] Chickens, turkeys, and other birds commonly acquire the disease after contact with moldy feed.

In the United States several clinical types of pulmonary aspergillosis have been described. The mildest form has been characterized by an acute tracheobronchitis, which usually runs a benign course.[2, 3] Cawley[4] and Gerstl and associates[5] described a severe pneumonic type which resulted in generalized aspergillosis and death. Chronic forms have also been described showing marked resemblance to tuberculosis[6] or neoplasm. Gerstl was the first to report a successful lobectomy for localized bronchopulmonary aspergillosis. This paper presents a report of the second case which resembled a neoplasm radiologically and which was successfully extirpated.

CASE REPORT

A 35-year-old, well-developed, white man was admitted to the hospital on May 2, 1949, with no complaints. Prior to induction into the Army in August, 1941, he was a salesman in a chicken-feed store. Subsequent to separation in August, 1945, he was actively engaged in chicken farming. According to the patient, a "spot" was seen on the x-ray film of his chest taken by a mobile unit two weeks before admission. He was referred to a near-by hospital where studies of the sputum for tumor cells and tubercle bacilli were negative. Bronchoscopic examination showed a normal tracheobronchial tree. He was then transferred to this hospital.

Past history revealed that he had had a bout of left lower chest pain with fever and a nonproductive cough in 1947, two weeks following a dental extraction. Four months later he had a severe cold with a hacking cough, productive of a small amount of yellowish sputum with occasional blood-streaking. These symptoms cleared after taking a sulfonamide drug. He was well until three months before admisssion when he developed another severe cold with the expectoration of a small amount of nonbloody sputum.

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Physical examination revealed a well-nourished patient who did not appear ill. Temperature was 98.6° F. and the pulse rate was 84 per minute. Examination of the lungs was negative. X-ray films of the chest revealed an ovoid area of infiltration about 4 cm. in diameter in the apical segment of the left lower lobe. There was a questionable high light in the region of this infiltration (Fig. 1).

Laboratory studies revealed that the red blood cell count was 4,800,000, hemoglobin 14.5 Gm., and the white blood cell count was 10,000. Tuberculin intradermal test (P.P.D.) was positive in the first strength. A coccidioidin skin test (1:1000) was negative. Sedimentation rate was 7 mm. per hour (Wintrobe). Sputum culture showed many streptococci, *Hemophilus influenzae*, diphtheroids, and staphylococci. Six concentrated specimens of the gastric juice were negative for tuberculosis and pathogenic fungi.

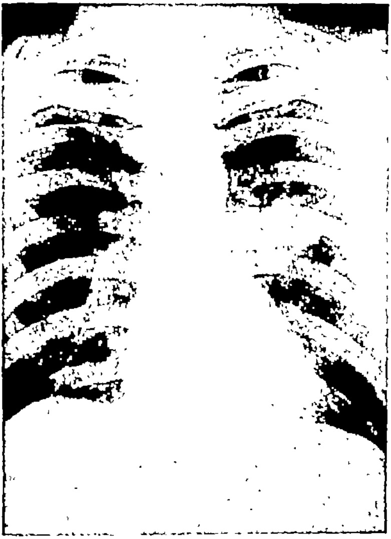

Fig. 1.—Anteroposterior view of lung reveals an ovoid area of infiltration in the apical division of the left lower lobe.

Clinical Course.—The patient remained asymptomatic and afebrile. Bronchoscopy again revealed a normal tracheobronchial tree. The differential diagnoses were chronic lung abscess, tuberculoma, and circumscribed carcinoma of the lung. On May 25, 1949, under endotracheal anesthesia the pleura was opened through the bed of the seventh rib. The lesion in the apical segment of the lower lobe was rounded and moderately firm and encroached upon the origin of the basilar bronchus. The fissure was developed with difficulty because of numerous vascular adhesions. The left lower lobe was removed by the technique of individual ligation of the vessels and the bronchus. A No. 26 catheter was inserted in the eighth interspace and the wound was closed in layers with silk. The patient was discharged on the ninth postoperative day after an uneventful recovery. He was completely asymptomatic when seen seven months later.

Pathology Report.—The specimen consisted of a pulmonary left lower lobe, measuring 17 by 17 by 2½ cm. and weighing 210 grams. A few fibrous tags were attached to the apex. The superior portion of the apical segment felt indurated and nodular. At a point 1½ cm.

from its origin, the apical bronchus opened into an irregular, partially loculated cavity, measuring 4 by 2 by 2½ cm. A branch of the apical bronchus also communicated separately with the cavity. The cavity was lined by a pink-tan, opalescent, smooth, glistening membrane, which was very easily separated from the cavity wall (Fig. 2). The wall was 2 mm. thick and smooth, except for a single, flat, irregular projection 1 cm. in diameter, which consisted of incompletely removed membrane. The parenchyma surrounding the cavity was indurated. On microscopic examination, the wall of the cavity was lined partially by pseudostratified ciliated columnar epithelium and partially by metaplastic squamous epithelium. There were also transitional ulcerated areas and re-epithelialized ulcerations covered by a single layer of cuboidal cells. Mucous glands, smooth muscle, and cartilaginous plates were found within the wall of the cavity which was fibrotic and heavily infiltrated with plasma cells, mac-

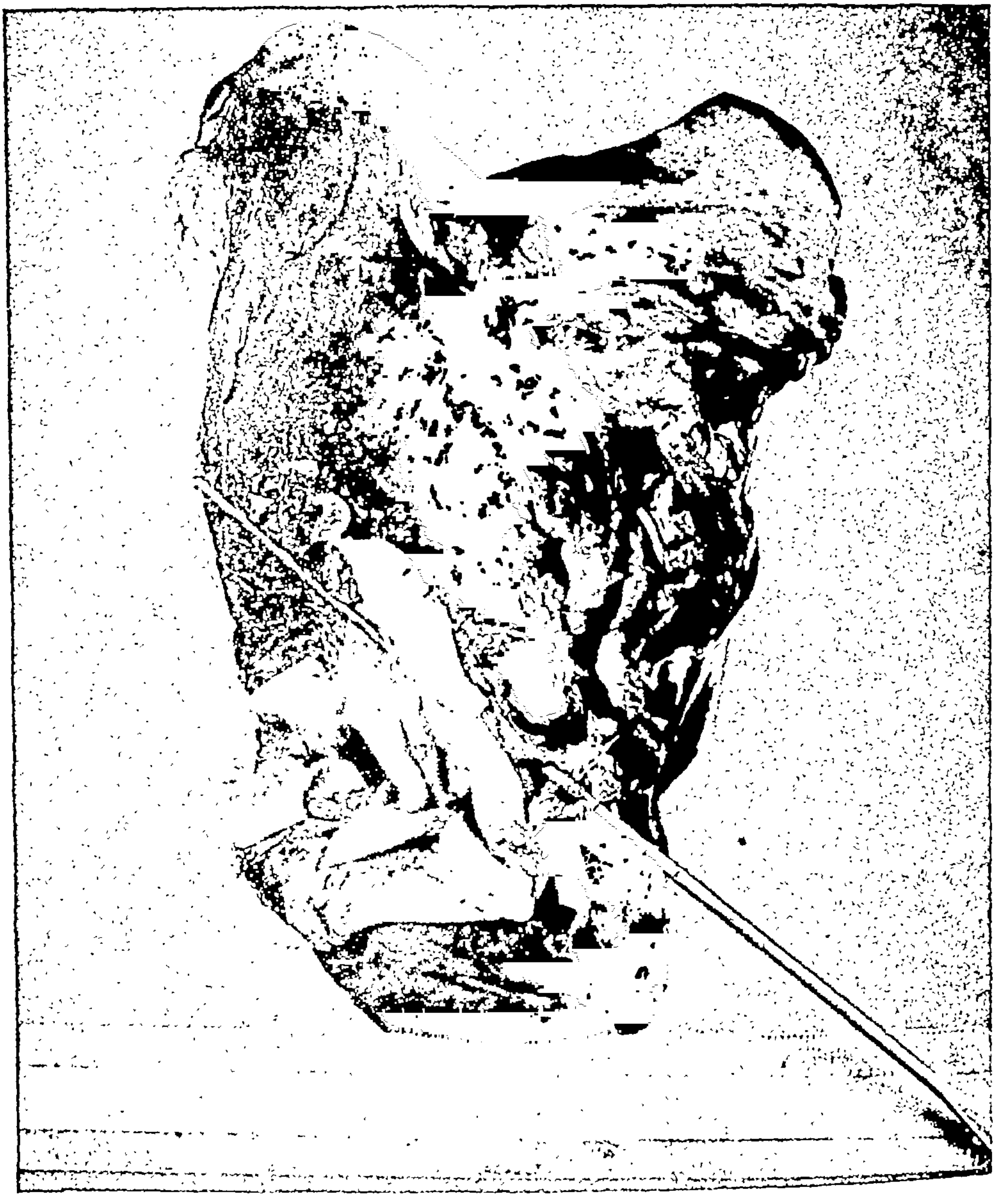

Fig. 2.—Lung specimen showing two bronchi entering the cavity which is filled with a lightly attached, glistening, opaque aspergillosis membrane.

rophages, eosinophiles, and polymorphonuclear leucocytes. The surrounding lung parenchyma was also chronically inflamed. The lymphocytic infiltration was organized in some areas into follicles, some of which contained germinal centers. The lining mucosa of the cavity was

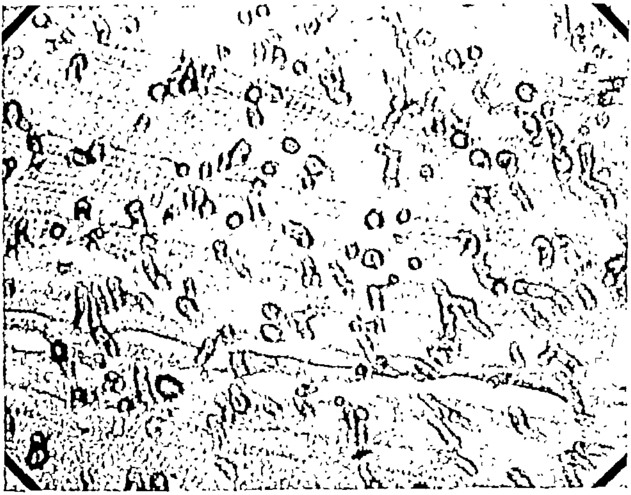

Fig. 3.—Oil immersion photomicrograph of mycelial membrane shown in Fig. 2.

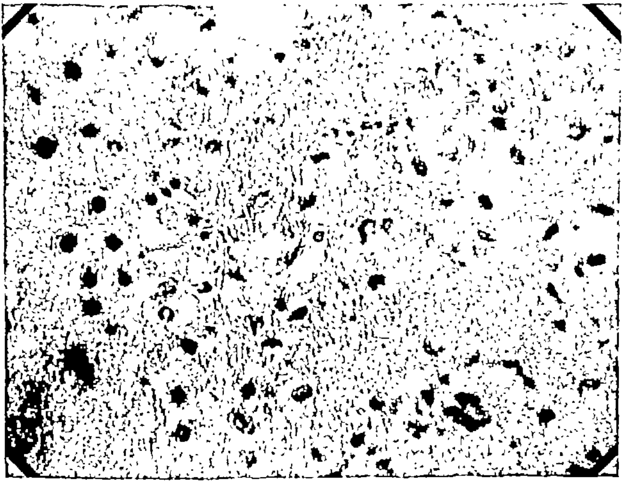

Fig. 4.—Oil immersion photomicrograph of thrombus containing mycelia in portal vein radicle of rabbit, produced by intravenous injection of suspension of aspergillus grown from membrane of patient's cavity.

frequently invaded by polymorphonuclear leucocytes. Granulation tissue was everywhere evident beneath the thickened basement membrane and fresh thrombi were attached to the ulcerated foci of the mucosa. Section through the lining membrane revealed a hyaline laminated structure, throughout which were present the branching mycelia of a fungus, frequently having the appearance of spores on cross-section (Fig. 3). On culture this membrane yielded a pure growth of colonies characteristic of aspergillus.* On June 19, 1949, a heavy saline suspension of the organisms was injected into the ear vein of a rabbit, which died in about forty-eight hours. Sections through the rabbit's lungs revealed marked congestion and edema and numerous small granulomas consisting of macrophages filled with small, round, foreign bodies consistent with spores. Some of these granulomas also showed foci of necrosis and polymorphonuclear leucocytic infiltration. Numerous fungal mycelia were present throughout the sinusoids of the liver, in which there were numerous foci of necrosis and thrombosed veins. Fungal mycelia were seen within the thrombi (Fig. 4). The most luxurious growth was found in the kidneys where large areas of necrosis occurred in conjunction with the growth and where blood vessels invaded by the fungi were also thrombosed. No fungi were noted in the spleen.

COMMENT

The gross and microscopic picture of the lesion, the demonstration of aspergillosis in the membrane lining the cavity, a positive virulence test in an inoculated rabbit, and the failure to demonstrate any other causative agent, are the reasons for considering this a case of primary bronchopulmonary aspergillosis. In addition, the patient was exposed to moldy feed in his occupation. Preexisting bronchiectasis is unlikely because more than one bronchus entered the cavity, as in Deve's[7] case, and the lesion was confined to the apical segment of the lower lobe, an unusual site for localized bronchiectasis. The possibility exists, however, that the aspergillosis was superimposed on a chronic lung abscess, secondary to the dental extraction of 1947.

Iodides and thymol have been efficacious in the treatment of the tracheobronchitic and tubercular forms of the disease. Surgical intervention should be employed as an effective measure in the treatment of localized bronchopulmonary aspergillosis.

SUMMARY

The third case of localized bronchopulmonary aspergillosis successfully treated by surgery has been reported. The patient has shown no clinical or x-ray evidence of recurrence of disease following operation.

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*The fungus was identified as *Aspergillus fumigatus fresenius* by Dorothy I. Fennell of the Fermentation Division, Northern Regional Research Laboratory, Peoria, Ill.

NEUROFIBROSARCOMA OF THE ANTERIOR MEDIASTINUM

SURGICAL REMOVAL

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IN A comprehensive review of the literature on "Mediastinal Tumors and Cysts" Thompson[1] found only two tumors of neurogenic origin arising in the anterior mediastinum. On the basis of observations in 135 mediastinal neurogenic tumors Blades[2] concluded that these tumors are almost always located in the posterior mediastinum. His collected series of cases consisted of 70 ganglioneuromas, 24 fibroblastomas, 22 neurofibromas, and 19 neurinomas.

The case to be presented in this paper is one of a neurofibroma which had undergone sarcomatous changes. It was located in the anterior superior mediastinum and was large enough to cause such critical tracheal compression that its removal was performed as an emergency procedure. Because of the rarity of this pathologic entity in the anterior mediastinum and the successful end result we feel that this case is worthy of report.

CASE REPORT

T. S., a 63-year-old gardener, entered Kings County Hospital on Jan. 4, 1947, with a ten-day history of dyspnea made worse three days before admission by an upper respiratory infection. Past history was noncontributory.

On admission to the hospital the patient was acutely sick, orthopneic, dyspneic, and cyanotic from the crown of the head down to the middle of the chest. The superficial veins in the neck and on the chest and abdomen were quite prominent. The pupils were dilated and reacted to light and accommodation. The right lobe of the thyroid appeared enlarged. There was fullness in the suprasternal notch and deviation of the trachea to the right. The anterior superior mediastinal region was widened to percussion for about one inch to either side of the sternum. The blood pressure in the right arm was 148/98 and 158/90 in the left arm. The remainder of the physical examination was essentially negative.

Radiographic examinations of the chest (Fig. 1) which included kymography and barium sulfate ingestion studies revealed a large anterior superior mediastinal mass which extended to both sides of the midline and upward into the neck. The lateral borders of the opacity were sharply demarcated from the surrounding tissues. The edges of the tumor were smooth and regular. There was considerable displacement of the trachea to the right. Kymographic studies did not show any pulsations within the mass. Fluoroscopy during barium sulfate ingestion showed the esophagus to be deviated to the right in the region of the tumor.

On admission to the hospital the patient was immediately placed in an oxygen tent. His condition improved during the next few days so as to permit investigation of the cause of his illness. The improvement, however, was not long lasting. On Jan. 22, 1947, he began to have respiratory distress even in the oxygen tent. The following day there was increased dyspnea and cyanosis. It was, therefore, deemed advisable to remove the tumor compressing the trachea as soon as possible. In view of the fact that the clinical diagnosis rested between (1) retrosternal thyroid and (2) primary anterior superior mediastinal tumor, it was felt

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that the fastest and least traumatic approach to the tumor would be through the neck. Accordingly, on Jan. 23, 1947, under endotracheal anesthesia, a collar incision was made at the base of the neck. After the thyroid gland had been exposed, a discrete nodule was found within the substance of the lower pole of the right gland. It was then noted that the tumor

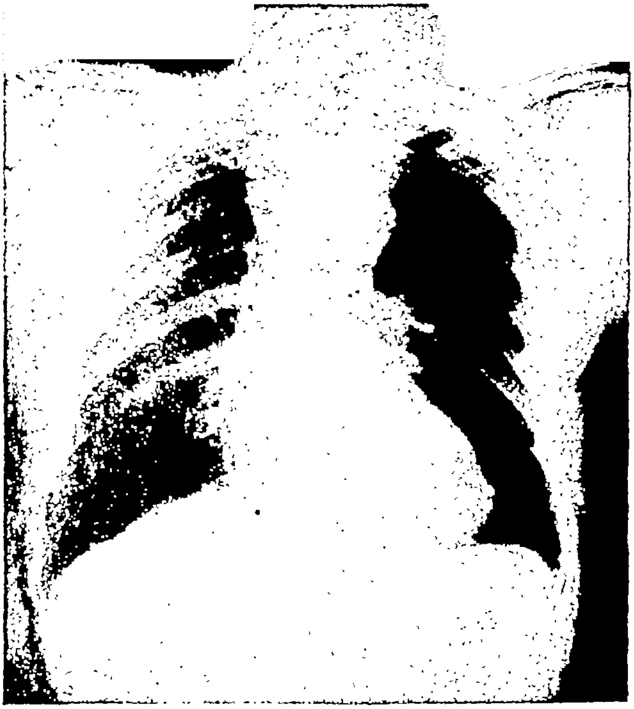


Fig. 1.—Roentgenogram of the chest taken on admission to the hospital. There is a large superior mediastinal shadow with deviation of the trachea to the right.

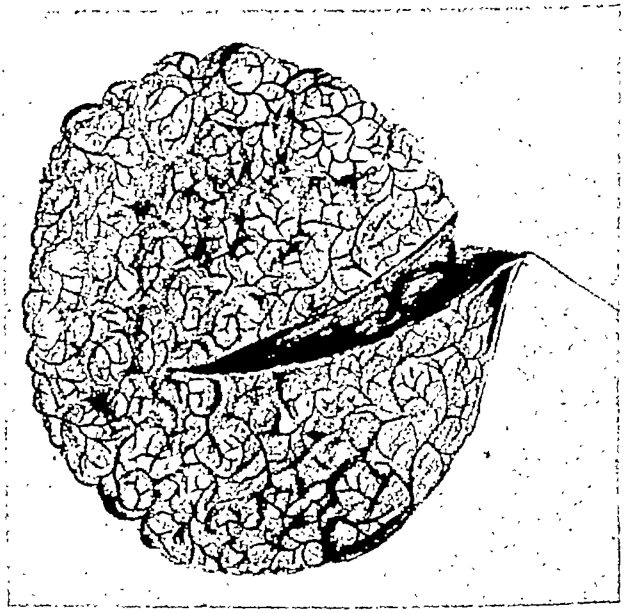
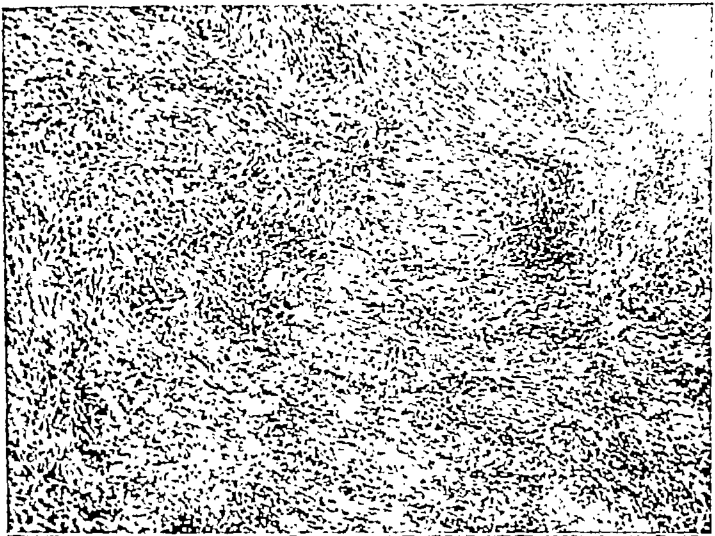


Fig. 2.—Drawing of the tumor removed from the anterior superior mediastinum. The tumor measured approximately four inches in diameter.

Fig. 3.



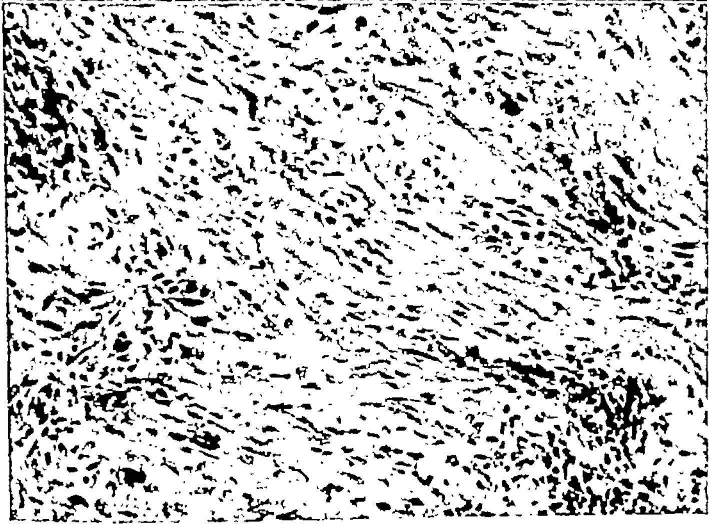


Fig. 4.

Fig. 3.—Photomicrograph of the tumor (magnification ×100) showing cytology of the tumor.

Fig. 4.—Photomicrograph of the tumor (magnification ×225) showing the deeply staining hyperchromatic markedly fasciculated structure of a neurofibrosarcoma.

in the mediastinum was *not* connected to the thyroid gland. The nodule within the thyroid gland was removed. Traction upon the mediastinal tumor in an attempt to deliver it into the neck produced marked respiratory distress, cyanosis, and elevation of the pulse rate. In order to decompress the mediastinum and relieve the pressure upon the trachea, the neck wound was abandoned and an incision made on the left side of the chest over the second rib anteriorly. About three inches of the cartilage and bone were removed. The tumor bulged through this opening and the patient's breasing imprvoed, the cyanosis diminished, and the pulse rate declined. After the patient received about ten minutes rest, the operation was resumed and the tumor removed through an opening in the left mediastinal reflection of pleura. The chest wall wound and the one in the neck were closed by coaptating the corresponding layers of tissue. The patient's immediate postoperative condition was fair. After the third postoperative day he showed steady and progressive improvement except for the development of an ischiorectal abscess which required incision and drainage on the sixth postoperative day.

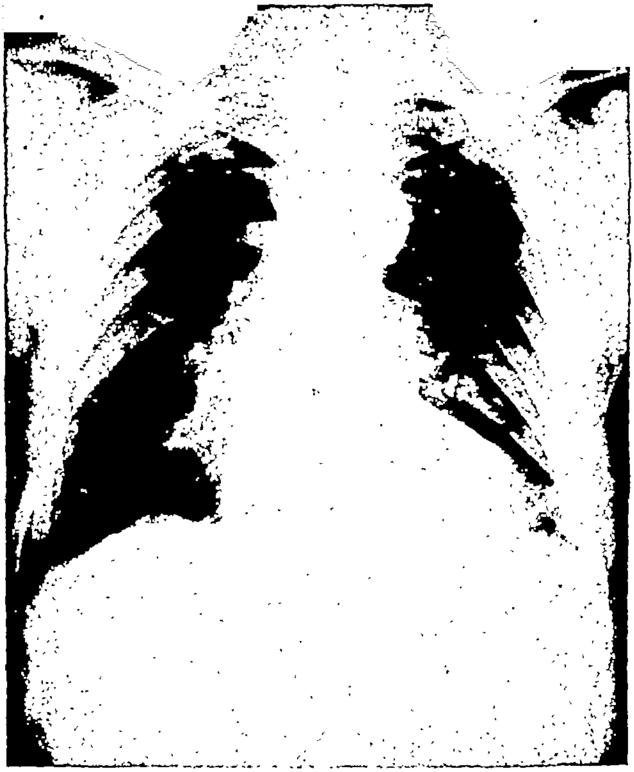


Fig. 5.—Roentgenogram of the chest taken two years after the removal of the mediastinal tumor.

Microscopy of the nodule removed from the thyroid gland showed adenomatous changes.

The tumor mass removed from the retrosternal region was described as follows: The mass was ovoid in shape and measured 4 by 3 inches in diameter (Fig. 2). *Microscopy* showed the presence of collagenous fibrous tissue with fasciculations. Many of the cells were elongated, large, and oval in shape with eccentric hyperchromatic large reticular nuclei. In some areas lymphocytic infiltration and calcification were noted (Figs. 3 and 4). The diagnosis was mediastinal neurofibrosarcoma.

The patient was discharged from the hospital two months after the operation on the chest. He was seen periodically in the Chest Clinic of this hospital, the last time being on Jan. 10, 1949 (Fig. 5). At that time he stated that he had gained considerable weight, that he had had no recurrence of symptoms or pain in the chest and that he had been working as a gardener and handyman ever since his discharge from the hospital. Because of his employment by the Kings County Hospital he has been seen frequently, outside of the clinic, and has remained well to date.

DISCUSSION

Heuer and Andrus[3] demonstrated that intrathoracic tumors of nerve tissue origin may arise from any of the nerve elements as well as from their sheaths or connective tissue contents. Another possible source of origin of these tumors is cell rests deposited ectopically during embryonic development which become active during later life. A review of the cases of neurofibromas and neurofibrosarcomas reported in the literature shows that they usually occur singly in the chest and probably arise from the connective tissue elements of nerve. In a review of 105 cases of intrathoracic neurogenic tumors Kent, Blades, Valle, and Graham[4] observed that 39 (37 per cent) were malignant. They also noted that neurogenic tumors arising within the mediastinum were less liable to malignancy than those originating in the more peripheral parts of the thorax. The average age of the patient in 55 cases of benign neurogenic tumor was approximately 26 years and in 15 cases of malignant tumors it was 17 years. Our patient did not conform with the observations of other writers either in location of the tumor or age of the patient.

The symptom complex in cases of neurogenic mediastinal tumors may take one of three forms—(1) neurologic, (2) manifestations of increased mediastinal pressure, and (3) pulmonary—one of which predominates. Not infrequently there is a combination of symptoms. Most writers believe that the onset of symptoms is chiefly neurologic and that encroachment upon the mediastinum and lung occurs late in the course of the expansion of the tumor. Harrington called attention to the fact that benign tumors are usually asymptomatic even when of considerable size, whereas severe intercostal pain was a common feature in malignant neurogenic tumors and in benign tumors undergoing malignant degeneration. All symptoms and signs of nerve involvement were absent in our patient. Interference with respiration due to pressure upon the trachea was the chief reason for considering the tumor preoperatively to be a retrosternal thyroid goiter. The bizarre symptomatology in our case was due to the unusual location of the neoplasm, that is, in the anterior superior mediastinum.

The roentgenologic findings in neurogenic mediastinal tumors usually consist of an area of mediastinal opacity the borders of which are smooth and more rarely lobulated. Occasionally there may be noted erosion of the osseous tissue in juxtaposition to the tumor. This is due to local pressure and does not indicate malignant transformation. In the lateral roentgenogram these tumors are usually found in the posterior mediastinum. In our case the tumor was located in the anterior mediastinum. Neither benign nor malignant tumors of neurogenic origin respond to x-ray therapy. The so-called "test dose" of deep roentgen rays is not warranted in mediastinal neurogenic tumors. The treatment of such tumors is surgical. The recent advances in thoracic surgery and anesthesiology have made exploratory thoracotomy a safe procedure. At the time of such intervention not only may the surgeon remove tissue for biopsy purposes but he may also remove the lesion, eradicating the disease.

RÉSUMÉ

A case is presented (with a three-year follow-up) in which a primary neurofibrosarcoma was removed from the anterior superior mediastinum. A brief discussion of mediastinal neurogenic tumors is also presented.

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CAVERNOUS HEMANGIOMA OF THE MEDIASTINUM

Case Report

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BECAUSE of the relative rarity of mediastinal tumors of blood vascular origin, such a case is believed suitable for recording.

A recent article from the Mayo Clinic* indicates that an extensive search of the literature on the subject reveals 14 acceptable cases of tumors of the mediastinum which are believed to be of blood vascular origin. The authors added to this series 3 more such cases, making a total of 17 authenticated cases of blood vascular tumors of the mediastinum. There was evidence of malignancy in 8 of the 14 cases gleaned from the literature and 2 of the 3 cases reported in the article showed evidence of malignancy. In the present case report the tumor showed no evidence of malignancy. The 3 cases at the Mayo Clinic occurred among approximately 200 patients with mediastinal tumors operated upon. The relative rarity of such tumors may be understood from this report.

Following is a case report of a similar tumor:

History.—Mrs. C. B., female, aged 18 years, presented herself for examination July 7, 1949. Patient stated that in 1939 she was treated for lobar pneumonia and responded well to one of the sulfonamides. An x-ray examination of the chest was made at that time, but it did not help because when it was taken it showed a homogeneous density obscuring the lower two-thirds of the left lung field, and if any tumor was present at that time it was well hidden by the pneumonic process. Otherwise, the history was noncontributory, consisting of the usual childhood diseases without any sequelae. In February, 1949, the patient was walking down the street in her home city when she noticed a mobile unit of the National Tuberculosis Association and had an x-ray examination made. She had no symptoms at that time that might be related to chest pathology. The physician in charge of the unit did not tell her what he had found but advised her to report to her private physician for examination and repeat x-ray examination. This was done and the examining physician found evidence of tumor which caused him to refer the patient for further examination and treatment. Following the original detection of the tumor, the patient in retrospect had the following complaints: vague distress in the left chest which came and went, bearing no relation to effort. No history of cough, hemoptysis, or weight loss. No dyspnea but fatigued easily. She had particularly noticed that she was unable to swim as well as she could several years ago because of the progressive shortness of breath.

Physical examination revealed no demonstrable abnormalities on careful examination of the entire chest. Blood pressure 120/78, pulse 74 per minute. Heart sounds entirely normal.

X-ray Examination, July 7, 1949.—Posteroanterior and lateral projections of the chest showed the right side essentially clear. The left side revealed a rounded mass extending from the hilum into the lung structure in the midportion of the lung field. Vertical diameter of the shadow was about 11 cm. Lateral borders were smooth in outline. Lateral view showed this mass to be located anteriorly and superimposed on the heart shadow. This tumor was interpreted as being a teratoid type of tumor in the left chest.

From the Thomas-Davis Clinic.
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*Seybold, W. D., McDonald, J. R., Clagett, O. T., and Harrington, S. W.: J. THORACIC SURG. 18: 503, 1949.

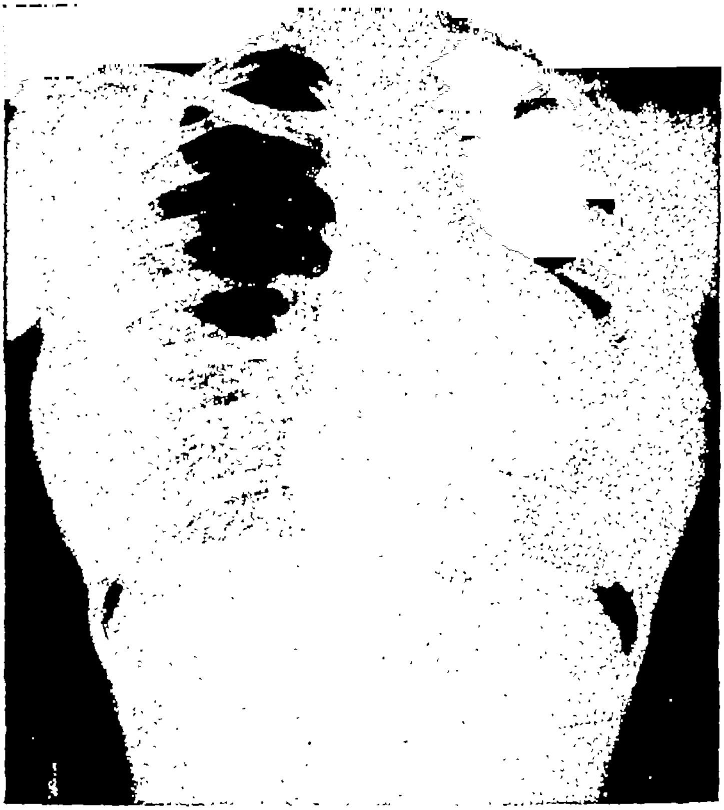

Fig. 1.—Posteroanterior chest preoperatively.

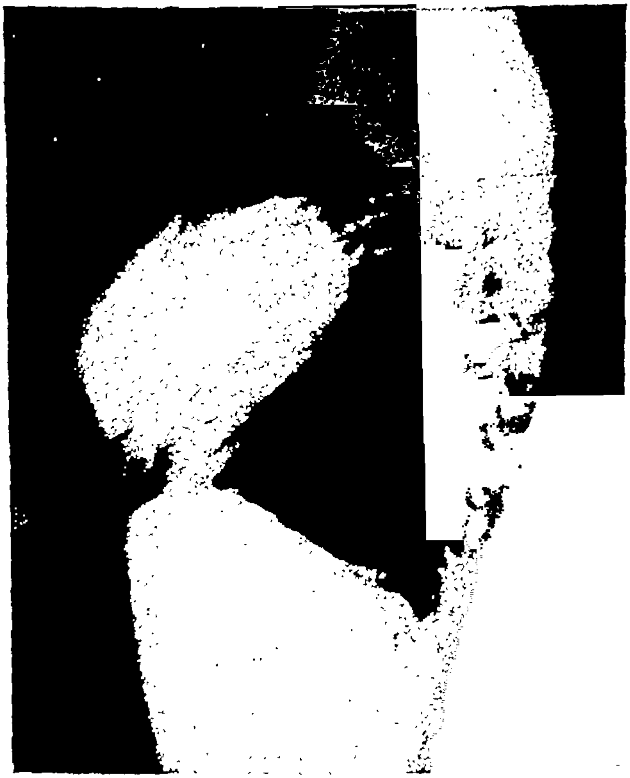

Fig. 2.—Lateral chest preoperatively.

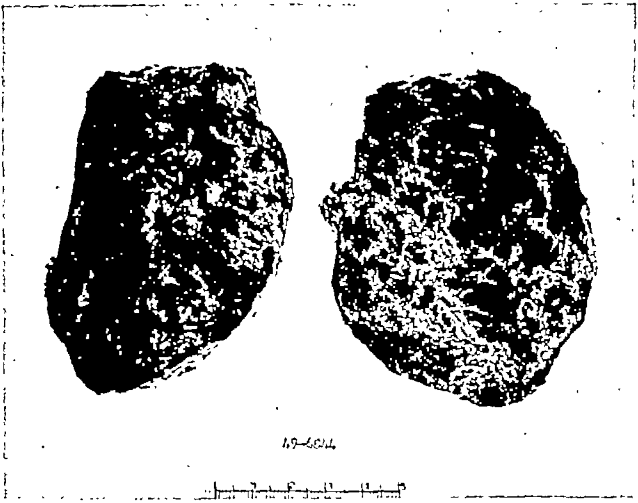

Fig. 3.—Description of illustration is contained within the text.

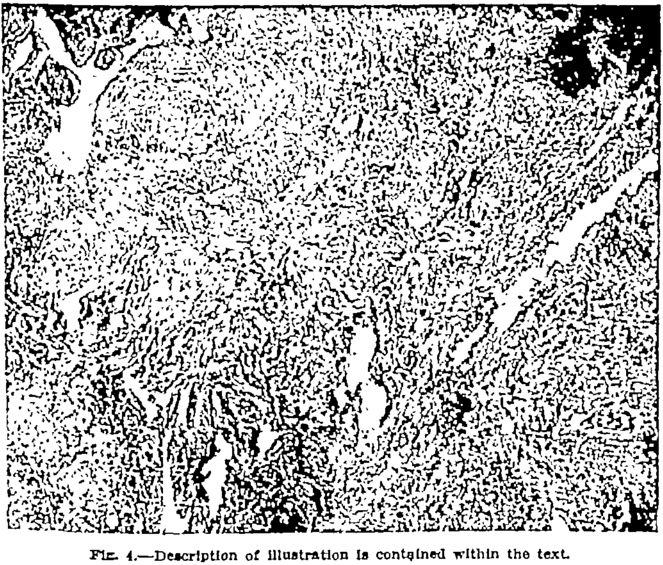

Fig. 4.—Description of illustration is contained within the text.

Operation, July 18, 1949.—Patient was subjected to exploratory thoracotomy on the left side, and after the lung had been retracted a large mass approximately 10 by 8 by 7 cm. in diameter was located on the left surface of the pericardium. The mass was not attached to the pericardium but seemed to be surrounded by its own capsule. The capsule was incised and the mass was dissected free from its capsular attachment with some difficulty. Dissection progressed to a pedicle approximately 2 cm. in diameter located near the arch of the aorta. The exact origin of the pedicle and the mass was not determined. The mass was removed at its pedicle and hemostasis was secured by suture ligatures. Operation was concluded by closing the thoracotomy incision with closed drainage. Patient made an uneventful recovery and was discharged on the seventh postoperative day.

Pathology Report.—Gross: A somewhat egg-shaped mass which weighed 275 grams, measured roughly 10 by 7.5 by 6.5 cm., and presented a shaggy surface. The mass did not appear to have been readily enucleated. When a section was carried through the mass, a large amount of blood escaped. The substance of the mass had a cavernous structure, blood escaped from the cavernous spaces.

Microscopic: The mass was made up predominantly of blood vascular elements which were often closely packed together. These blood vessels varied markedly in size and in thickness of their walls, the smaller channels were hardly larger than capillary size and possessed walls of capillary thinness. The larger cavernous spaces occasionally possessed relatively thick walls apparently made up chiefly of smooth muscle fibers. The stroma was not richly cellular and was made up of well-differentiated connective tissue, in which there were imbedded rather numerous scattered aggregations of lymphoid cells, apparently inflammatory cells since there was no arrangement of these cells to form typical lymph follicles. No epithelial cells were seen. The various elements were well differentiated. There was no evidence of rapid growth.

Diagnosis.—Large cavernous hemangioma of the mediastinum.

DISCUSSION

A case is presented of a large cavernous hemangioma of the mediastinum occurring in an 18-year-old girl. The symptoms had been so mild as to not cause the patient to seek medical help but accidental discovery and questioning by her local physician brought out mild pressure symptoms dating for approximately one year prior to the time of first examination. The tumor was removed and the patient made an uneventful recovery, leaving the hospital on the seventh postoperative day. Pathologic report on the tumor placed it in a class of mediastinal tumors of blood vascular origin of which relatively few have been reported in the entire literature. Surgery in this case should result in a permanent cure.

SOME ASPECTS OF CAVITY BEHAVIOR IN PULMONARY TUBERCULOSIS

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DESPITE years of close study and therapeutic attacks from many angles, the tuberculous pulmonary cavity continues to be one of the most difficult problems to confront the clinician, by reason of its unpredictable response to treatment.

Of the modern active methods of cavity treatment, namely, collapse therapy, transpleural drainage, and lung resection, the latter is being employed ever more frequently, particularly for those cases which have not responded to the other two less radical forms of therapy. Many cases of advanced bilateral disease, however, are not suitable for lung resection.

Collapse therapy is a well-tried method of treatment which has been attended by a high percentage of successful results. On the other hand, many cases have their chances of survival lessened by very extensive, perhaps overenthusiastic collapse therapy, sacrificing badly needed lung function. This is done in an attempt to force cavity obliteration by extensive irreversible lung collapse through multiple rib resection.

Transpleural cavity drainage is a useful method particularly in conjunction with collapse therapy for large cavities. This procedure, particularly in the closed form, however, is sometimes hazardous to institute because of uncertainty as to the adequacy of pleural space obliteration, and the lack of a sure closed method for bringing about such obliteration.

In the belief that each of the methods mentioned has its place in cavity treatment at the appropriate time, and that the proper method can be best selected for any particular cavity by studying the type of cavity or phase of cavity evolution with which one is dealing, it is suggested that closer attention to cavity behavior than merely the establishment of the existence of a cavity is required for intelligent application of the methods. The need for such cavity study is well recognized. The work of Pearson, Eloesser, Monaldi, Coryllos, Vineberg, Kunstler, and others drew attention to the blocked cavity or "positive pressure cavity," and suggested transpleural drainage for its treatment.

In this article certain aspects of the behavior of cavities, particularly under the conditions of lung collapse and lung expansion, will be discussed. Some experiences with a plan of procedure aimed primarily at the most efficient and lung-sparing use of collapse therapy, but providing at the same time for the safe use of transpleural drainage or the early institution of lung resection, will be described.

Cavity Persistence.—The mechanism of formation of a tuberculous lung cavity is fairly well understood, but the cause or causes of cavity persistence are still debatable. With our present knowledge, one may assume that aside from

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immune-biologic considerations, there are at least two important causes of cavity persistence, of a mechanical nature, which might be called: (1) cavity fixation, and (2) cavity inflation.

By cavity fixation is meant rigidity of the cavity wall due to fibrosis, and also adherence of the surrounding diseased lung to the resistant bony parietes.

By cavity inflation is meant the progressive trapping of air and the products of tissue destruction within the cavity due to a stop-valve effect in the drainage bronchus or bronchi.

Cavity Obliteration.—The mechanism of cavity obliteration, whether spontaneously or under collapse treatment, is not clearly understood. The most direct form of attack on cavity fixation would seem to be collapse therapy by removal of ribs or division of adhesions. Similarly the most direct treatment for cavity inflation should be adequate cavity drainage either in the natural way through the bronchus or by surgical intervention transpleurally.

If the cavity wall and the surrounding lung have become sufficiently rigid with fibrous tissue and calcification, then probably neither collapse nor transpleural drainage, nor any combination of these will cause cavity obliteration. The only effective remedy that one can see for such a cavity is complete eradication by lung resection.

In so far as the mechanism of cavity inflation is concerned, there is no need to postulate hinged flaps or other bizarre trap-door devices in order to produce a stop-valve effect. Partial occlusion of the bronchial lumen by thick secretions on inspiration can easily become complete occlusion on expiration, owing to the enlargement and diminution of the bronchial lumen accompanying inspiration and expiration, respectively. Such things as increased amount of secretion, semisolid or very viscid secretion, narrowing of the bronchial lumen by endobronchial disease, traction on the bronchial wall by fibrous tissue, compression of the bronchus by lung collapse, and increased inspiratory effort as in coughing or physical exertion will clearly favor cavity inflation. Conversely, thinning of the consistency of the secretion or reduction of its amount as after periods of treatment, or reduced inspiratory effort through bed rest, or sedation of useless cough, will lead to diminished cavity inflation, or deflation and occasionally even cavity disappearance.

Hence, it would appear that the phasic character of cavity inflation with periods of increase in size often alternating with periods of decrease in size can be readily explained on the basis of variation in effective bronchial lumen and resulting bronchial drainage.

Cavity Treatment.—While in treatment, cavity inflation is most directly countered by transpleural drainage, and cavity fixation by collapse, it is clear that collapse therapy alone often deals effectively with cavity inflation. Everybody has experience of giant cavities exhibiting obvious signs of inflation including positive pressure and fluid levels, that have gone on to obliteration under collapse therapy without the added assistance of transpleural cavity drainage. This may be at least partly explained by the fact that collapse therapy generally diminishes the amount of air entering the cavity.

This is particularly true of one form of collapse therapy, namely, diaphragmatic paralysis. This procedure puts out of action the bellows effect of the contracting diaphragm, thus reducing the amount of air entering the lung and the cavity at each inspiration. It is possible that this is the most effective factor in diaphragmatic paralysis and not the diminution in lung volume resulting from diaphragmatic ascent. The rapidity with which some lower and midlung cavities disappear after phrenic interruption even with only slight rise of the diaphragm bears out this contention. Inflated cavities exhibiting positive pressures have been seen to disappear after phrenic interruption without transpleural drainage.

In the same way, for upper lung cavities one need not always require drastic reduction in lung volume, with corresponding loss of lung function, in order to secure cavity obliteration. Removal of a few of the upper ribs, or the creation of an air- or fluid-filled space around the upper lung hinders the inspiratory action of the costosternal mechanism and thus diminishes cavity inflation, often resulting in cavity disappearance.

It is unfortunate that the reduction in lung volume caused by collapse means a corresponding reduction in the lumen of the smaller muscle-walled bronchi, and hence interferes with bronchial drainage and favors cavity inflation. In fact, it is quite possible that too great a degree of collapse may in this way, paradoxically, favor cavity persistence. This is seen at times in cases of pneumothorax where all adhesions have been divided and despite optimum concentric collapse the cavity, instead of diminishing, retains its original size or even enlarges. Frequently on permitting the lung to re-expand in such cases, the cavity diminishes and at times disappears (Case 1).

In theory the correct amount of collapse is that which eliminates adherence of the lung to the parietes, giving full scope to the contracting tendency of the fibrous tissue surrounding the cavity, without leading to compression and obstruction of the bronchial lumen. The rapid succession of stages as followed in the classical thoracoplasty, takes little account of this problem of bronchial drainage, and seeks to cause cavity obliteration by sheer reduction of lung volume. The fact that cavities sometimes persist despite extensive rib and transverse process resection, resulting in total lung collapse with corresponding severe and permanent loss of lung function not to speak of physical deformity, raises a question as to the soundness of such a proceeding. Moreover, after a two- or three-stage thoracoplasty, the residual cavity lies so inaccessibly close to the mediastinum that cavity drainage becomes impractical and lung resection remains the only hope. It is felt that the tendency in recent years has been to concentrate too much on the early ridding of the patient of a few tubercle bacilli from the sputum and not enough on preserving adequate lung function so that the patient can carry on a normal existence. To paraphrase Pinner, patients have been cured of their tuberculosis but cannot walk upstairs.

In an attempt to rationalize collapse therapy according to the principles outlined previously, and, above all, scrupulously to preserve lung function, a procedure has been tried over the past four years on a small series of 15 cases, resection of the posterior ribs. Should cavity rupture actually occur, one should probably remove the upper lobe, if possible, in order to avoid continuing feeding of the infection of the apicolysis space. Should this prove impractical because of the risk, open drainage of the apicolysis space with streptomycin aid seems a possible alternative. It is believed that average care and gentle dissection will prevent cavity rupture if one is alive to the danger and is ready to desist if rupture appears imminent.

The second difficulty concerns the danger of paradoxical respiration owing to the large area of unsupported decostalized chest wall left anteriorly after resection of the upper three ribs and costal cartilages. Support of the infraclavicular region with a large pressure pad hitched to the opposite shoulder and filling of the apicolysis space with normal saline have proved quite satisfactory in overcoming this problem. The pressure pad is kept in position for two weeks after the operation. Experience with resection of the anterior portions of the ribs with and without apicolysis has suggested that there is less trouble with paradoxical movement, when apicolysis is done. This causes complete collapse of the portion of lung underlying the decostalized chest wall, and largely prevents its taking part in respiratory movement. Filling the apicolysis space with saline further helps by supporting the chest wall and compressing the lung.

A further problem arises when a large cavity has been reduced in size by the anterior operation and then shows evidence again of an active inflation mechanism, in a new increase in size, suggesting the need for transpleural drainage. In that the cavity is now more deepseated in its lower position in the more roomy lower chest cavity, and because of its smaller size, its localization for drainage may prove difficult. After unpleasant experience with one such cavity where repeated needle explorations were followed by a fatal hemoptysis, drainage is not now attempted in any such cavity measuring under 4 cm. in diameter. Lung resection is preferred for such a cavity showing a pronounced inflation mechanism or if the inflation element is not marked, further collapse is tried through posterior rib resection.

To counterbalance the aforementioned disadvantages, this procedure seems to have certain advantages over the standard form of thoracoplasty which might be briefly summarized.

1. The patient is operated upon in the supine position for anterior thoracoplasty. This has an advantage for patients with large cavities and profuse sputum in that there is less danger of flooding of the opposite lung than if the patient were lying in the lateral position used in posterior thoracoplasty.

2. For anterior thoracoplasty a short incision is used extending from the midline to the midaxilla at the level of the second rib. The lateral half of the pectoralis major is divided between clamps and the medial half is split. With this approach there is much less blood loss th[illegible] with the first-stage posterior thoracoplasty.

3. Owing to removal of the wide[illegible] f the upper three ribs and their costal cartilages in thei[illegible] is provided by this operation than by the first-[illegible]

4. Only one operation with no deformity, little or no interference with shoulder function, and minimal reduction of lung function for those patients whose cavities go on to complete obliteration after the anterior operation.

5. Obliteration of the pleural space anteriorly in preparation for transpleural drainage should this prove necessary.. Both layers of the pleura become fused with the fibrinous deposit which forms in the apicolysis space postoperatively.

Fig. 1.

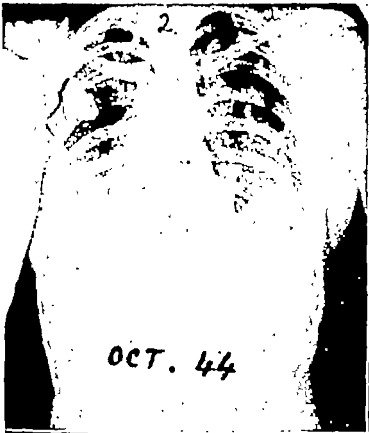
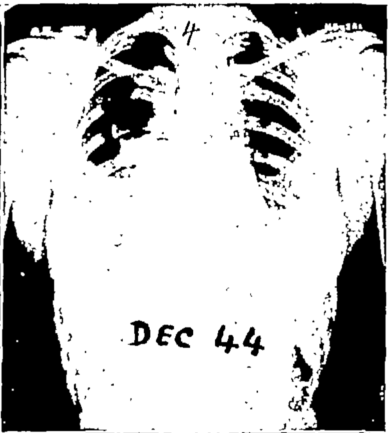


Fig. 2.



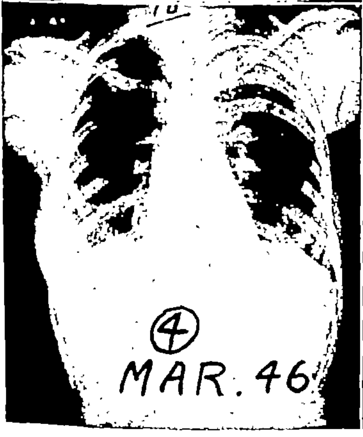


Fig. 3.

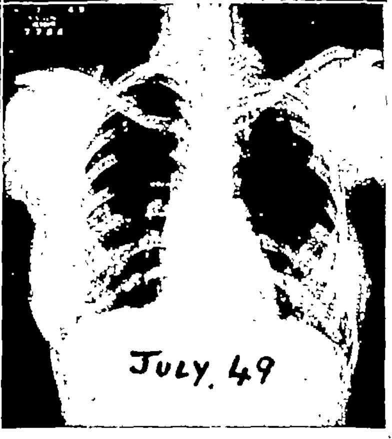


Fig. 4.

Figs. 1, 2, 3, and 4 (Case 1).—Typical of Group 1 type of cavity behavior.

CASE REPORTS

CASE 1.—Miss J. K., 21 years of age. Onset of pulmonary tuberculosis in June, 1944. Admitted Grace Dart Hospital September, 1944, with 6.5 cm. cavity in both upper zones.

October, 1944, left pneumothorax unsuccessful because of indivisible adhesions, and abandoned. November, 1944, right pneumothorax.

Fig. 5. Fig. 6.

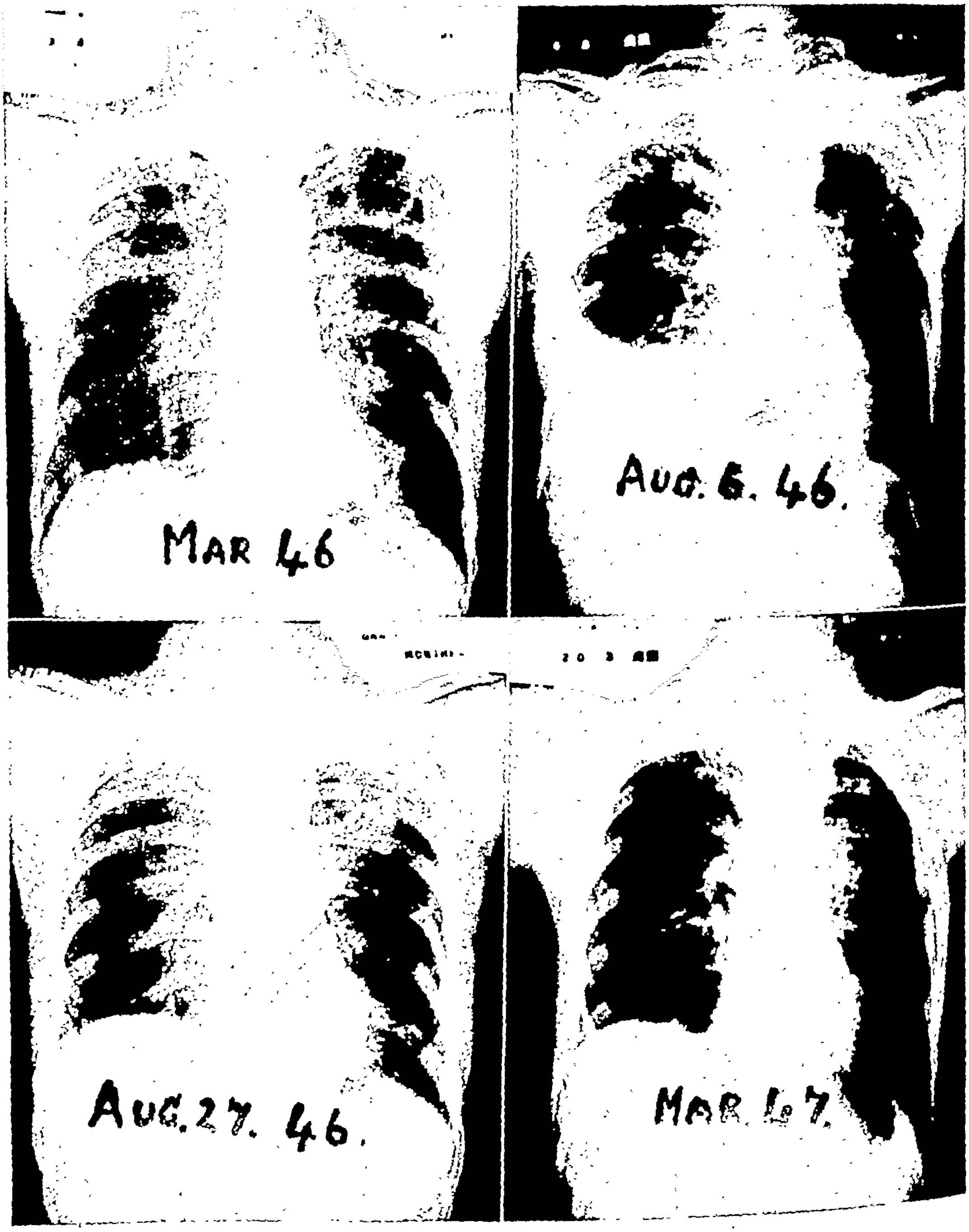


Fig. 7. Fig. 8.

Figs. 5, 6, 7, and 8 (Case 2).—Typical of Group 2 type of cavity behavior.

December, 1944, closed pneumonolysis with division of adhesions and good pneumothorax. The cavity, however, remained as large as before, and the pneumothorax was therefore abandoned. The cavity showed slow reduction in size and gradually disappeared. Cavity pressures were taken in this cavity in August, 1945, after the pneumothorax had become completely absorbed but while the cavity was still a fair size. Pressures were –5, –1 cm. of water. This is interesting in that the behavior of the cavity when it failed to become obliterated under a good pneumothorax suggested that it was in an inflated or positive pressure phase at that

Fig. 9. Fig. 10.

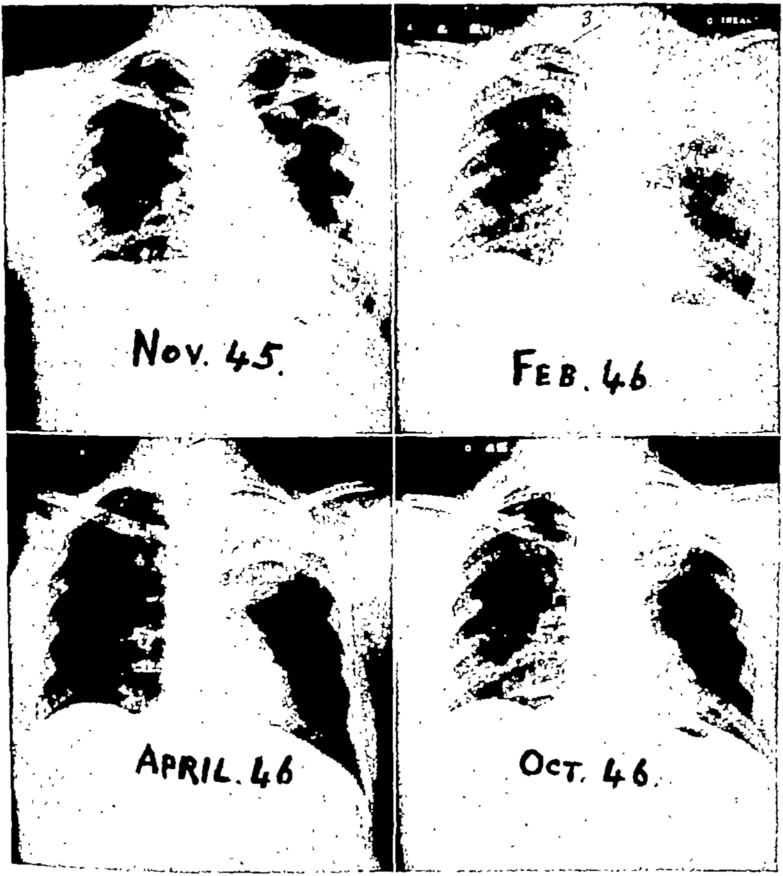


Fig. 11. Fig. 12.

Figs. 9, 10, 11, and 12 (Case 3).—Typical of Group 3 type of cavity behavior.

time. The history of this cavity, going on to obliteration on re-expansion after a period of collapse, suggested a similar course of treatment for the left-sided cavity. Cavity pressures on the left side in March, 1945, were 0, +3 and in December, 1945, were +½, +4.

In January, 1946, left anterior thoracoplasty with apicolysis was done. Sputum became negative in March, 1946, and has remained so. Tomogram has failed to show a cavity in either lung since April, 1946. Discharged in September, 1946. Has since married and has had children.

CASE 2.—Mr. C. R., 44 years of age. Onset of pulmonary tuberculosis in June, 1945. Admitted to Grace Dart Hospital in December, 1945, with 6.5 cm. cavity in left upper zone and 2 cm. cavity in right upper zone.

July 10, 1946, left anterior thoracoplasty with apicolysis.

July 31, 1946, right anterior thoracoplasty with apicolysis. The left-sided cavity was smaller in size after the operation, and then remained unchanged for three weeks after which it rapidly became reduced in size until on Aug. 17, 1946, it measured only 1½ cm. in its longest diameter. It failed to get any smaller over the succeeding three months so that a posterior thoracoplasty with resection of ribs four and five was done in December, 1946. The sputum became negative in October, 1946, and has remained so. Since March, 1947, there has been no conclusive evidence of cavity in the right upper lung.

Discharged in November, 1947. Working as a taxi driver.

CASE 3.—Mr. E. G., 33 years of age. Onset of pulmonary tuberculosis in 1942. Admitted to Grace Dart Hospital in December, 1945. Good chronic with 5.5 cm. cavity in the left upper lung.

Anterior thoracoplasty with apicolysis in February, 1946. Cavity was reduced to 3 cm., after the operation, but rapidly re-enlarged again to 4.5 cm. Transpleural drainage of cavity in April, 1946. Sputum then became negative and remained so until December, 1946, when sputum became positive again. Accordingly posterior thoracoplasty (ribs four, five, six, and seven) in January, 1947. Sputum negative since January, 1947. Discharged August, 1947.

RESULTS

Obviously no valid conclusions as to statistical evaluation of effectiveness can be drawn from a group of sixteen cavities in fifteen patients (one patient was operated upon bilaterally). The results are given in the hope that others may be stimulated by them to adopt similar studies in cavity behavior.

Of the sixteen cavities studied, all but three were 5 cm. or over in diameter and four were in the giant cavity class. It is thought likely that if smaller cavities were included a higher proportion of successful results would have been secured, and that many of the smaller cavities would have gone on to obliteration after the anterior operation without further interference. Smaller cavities are now being treated in this way and will be reported upon, when a sufficient time interval has elapsed to make the results worth while recording.

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degree of control of the first lesion and a more deliberate selection of the treatment for the second.

Admittedly, the possibility of survival diminishes with the advent of each new cancer capable of metastasizing. Yet, it is more and more suggestive, as experience accumulates, that the maintenance of aggression in treatment, rather than the yielding to defeatism, has produced surprisingly favorable results. Consequently, we feel that the appearance of two, three, or more primary cancers of different organ systems should not contraindicate radical therapy for each. If, for example, an adenocarcinoma of the rectum has been controlled by an abdominoperineal resection and later a carcinoma of the breast develops, it should be treated by radical mastectomy. Similarly, the apparently complete eradication of a malignant testicular tumor several years prior to the appearance of a gastric cancer would not contraindicate gastrectomy.

The probability of survival in each separate case of cancer varies considerably with the particular clinical setting. If the carcinoma of the rectum just mentioned occurred by itself and were in the pathologic classification of Duke's A or Duke's B, the patient would have an estimated 65 to 85 per cent chance of living five years. If the breast cancer that was removed subsequently were the only tumor present and found not to have metastases in the regional lymph nodes, the chance of five-year survival would be approximately 75 per cent. One can only conjecture whether the combination of these two primary lesions in one individual would alter the prognosis. Actually, it may be even better than that reported for cases in which only solitary cancer of the stomach or lung is present.

Patients need psychological help in facing repeated major surgical procedures, but respond well when a reasonable chance of "cure" is offered. Thus, a 49-year-old mother of four children did not protest when she was faced with the necessity of a radical mastectomy, an anterior resection of the sigmoid colon, and a right upper and middle lobe lobectomy—the last two operations within two months of each other.

CRITERIA FOR MULTIPLICITY

Criteria for diagnosis of multiple cancers must be clearly defined. In the first two examples cited previously, carcinoma of the rectum followed by a breast cancer and a malignant testicular tumor followed by a gastric cancer, the combinations of lesions were such that the second primary, because of its location, was not likely to be confused with a metastasis from the first. However, when lung tumors are considered, a careful distinction must be made as to whether this organ is acting as the site of a new growth or as a filter and repository of metastases. This distinction can be made only when the two tumors have entirely different histologic characteristics, as in Case No. 11 (Table III) in which a squamous carcinoma of the hard palate coexisted with an adenocarcinoma of the lung (Fig. 1). There are seven cases in this series meeting this criterion, and these are classified as having *positive* evidence of multiple primary cancers.

On the other hand, if the two lesions in question have the same histologic pattern, it is almost impossible to distinguish microscopically between a primary focus and a metastasis in the lung. By no means, however, does this necessarily exclude the possibility that the pulmonary lesion may be a separate and distinct primary. Reliance in these instances must be placed upon the clinicopathologic picture, and in this series, thirteen cases are classified as having *probable* evidence of multiple primary cancers. In Case No. 20, squamous carcinoma existed synchronously in the extrinsic larynx and the left main bronchus. The latter is an unusual site for metastasis from the former, and, in the gross specimen removed by total pneumonectomy, a cancer was found arising from the bronchial wall. There were no metastases noted in the remainder of the resected lung, nor have any appeared in the regional lymph nodes or in the opposite lung in the twelve months since operation.

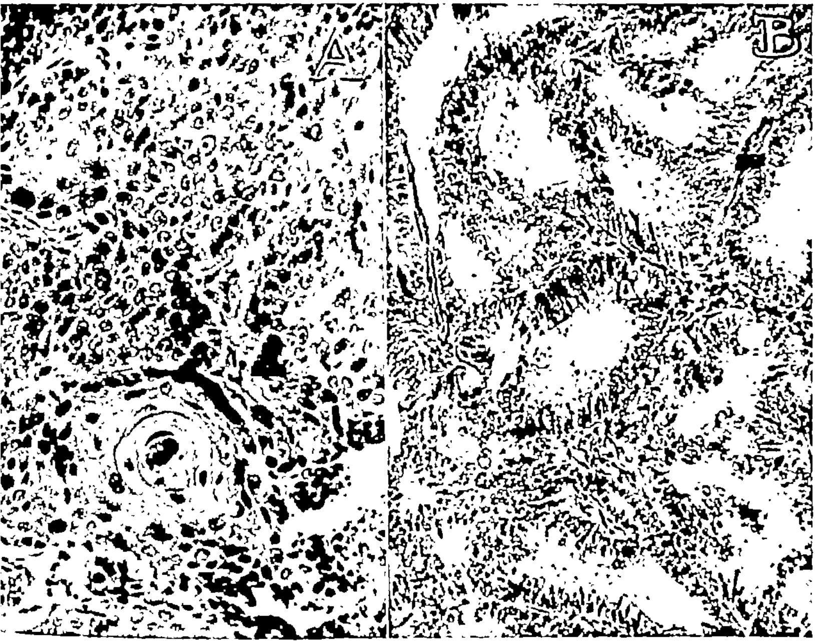

Fig. 1 (Case No. 11).—*A*, Squamous carcinoma of the hard palate, and *B*, adenocarcinoma of the lung, in the same patient.

In Case No. 13, a squamous carcinoma confined to the edge of one vocal cord and noninfiltrative in character, occurred synchronously with an epidermoid carcinoma of the right upper lobe bronchus. The pathologist felt that the probability that the two lesions represented a primary cancer and its metastasis was remote, despite the presence of the same basic histologic pattern.

In a separate group are five cases of lung cancer associated with basal cell carcinomas of the skin. Although these skin cancers are nonmetastasizing, their presence in combination with another malignant growth stresses the possible inherent tendency of some individuals to evolve cancer.

COMPILATION OF CASES

In 1,493 cases of cancer of the lung observed in Memorial Hospital over a period of twenty-four years, there have been twenty-five instances in which the lung tumor was one of two or more separate primary malignant growths—an incidence of 1.6 per cent (Table I). There was one triple primary. Warren and Gates[7] found 120 lung cancers in their autopsy series, in nine of which there was another primary lesion—an incidence of 7.5 per cent. The constituted 4.6 per cent of all the cases found at autopsy to have multiple primary cancers.

TABLE I. MULTIPLE PRIMARIES ASSOCIATED WITH LUNG CANCER
From the Files of Memorial Hospital

Total cases of lung carcinoma	1,493
Total multiple primaries	25
Incidence	1.6%

The sites of the separate malignant growths in our series are listed in Table II and include seven of the oral cavity, four of the larynx, two of the rectum, and one each of the breast, uterus, bladder, kidney, and thyroid. There was one case in which the lung cancer was combined with lymphatic leucemia and five cases where it occurred with basal cell carcinomas of the skin. The triple primary included cancers of the breast and sigmoid and is listed separately.

TABLE II. MULTIPLE PRIMARIES ASSOCIATED WITH LUNG CANCER

	DOUBLE PRIMARY
Oral cavity	7
Skin	5
Larynx	4
Rectum	2
Kidney	1
Bladder	1
Breast	1
Uterus	1
Thyroid	1
Lymphatic leucemia	1
Total	24
	TRIPLE PRIMARY
Breast and sigmoid	1
Total Cases	25

In the literature[5, 6, 7, 8] there are at least thirty-seven cases in which, at autopsy, a cancer of the lung has been found to be one of two malignant tumors; of these the kidney, colon, and stomach were the sites of the other tumor five times; the skin, four times; the prostate and breast, three times each; the esophagus, gall bladder, and tongue, twice each; and the lip, bladder, larynx, liver, sarcoma of the leg, and lymphosarcoma, once each. In addition, there was a triple primary arising synchronously as a squamous carcinoma of the bronchus, adenocarcinoma of the pancreas, and carcinoma of the prostate.

In a discussion of multiple primary malignant growths, the time relationships between the appearances of the tumors is of interest. In this communication, the cancers are considered synchronous if the interval between the establishment of the diagnosis of the first primary tumor and the detection of the second was less than six months; metachronous, if more than six months. In our twenty-five cases, the lung cancer was synchronous with another malignant tumor in fifteen instances—twelve of these in combination with a cancer capable of *metastasizing*—and in ten cases, the lung cancer appeared at least twelve months after the discovery of the first tumor. In not one instance did the lung lesion antedate the appearance of the second growth by any significant length of time, probably because the early mortality of patients with cancer of the lung precluded their propagating second lesions. This situation occurs also among the cases reported in the literature, in which the lung tumor was usually the last of the primary growths to appear in an individual.

DIAGNOSIS

When a patient who has a cancer known to metastasize develops pulmonary symptoms or an asymptomatic roentgenographic shadow suggestive of primary lung cancer, the problem of establishing the true nature of the process is vital and often requires considerable clinical and laboratory data.

History and Physical Examination.—In only one case was mention made of cancer in a member of the immediate family, but this item on the patients' histories was usually incomplete.

Although a primary cancer of the lung may be expected to show earlier evidences of bronchial irritation and compression than a metastasis, little reliance can be placed on signs and symptoms as aids in differentiating between the two. In this series, it was largely in the metachronous lesions that the symptoms of cough and hemoptysis directed attention to the lung.

There were twenty men and five women in this series. Their ages varied from 49 to 80 years, with an average of 62 years. The youngest patient was a 49-year-old woman who had three separate primary tumors.

Roentgenographic Findings.—Eight cases were detected following routine roentgenograms of the chest taken either as part of a check-up examination or to determine whether multiple lung metastases were present. The value of chest films at six or twelve-month intervals as part of a follow-up system cannot be overestimated.[4] Lesions discovered before symptoms develop are more likely to be resectable.

The correct diagnosis was suggested roentgenographically in ten instances. Primary lung cancer was suspected for the following reasons: the infrequency with which certain cancers metastasize to the lung, and the shape of the shadow, usually associated with a segmental atelectasis. It is felt, however, that the most important element is the alertness of the radiologist to the fact that a density in the lung *may* represent a new primary carcinoma and not necessarily a metastasis.

TABLE III

NAME AGE SEX	FAMILY HISTORY (CA.)	FIRST PRIMARY					LUNG PRIMARY				
		PATHOLOGY	SITE	YEAR TREATED	METHOD	TIME INTERVAL (YEARS)	FIRST SYMPTOM	DIAGNOSIS ESTABLISHED	PATHOLOGY	TREATMENT	FOLLOW-UP
Metachronous Multiple Primaries											
1. W. H. 54 M	+	Adenoca. gr. 3 nodes clear	Rectum	1940	A-P resection	8	Hemoptysis	Pap. IV, x-ray	Bronchiogenic Ca. nodes clear	Pneumonectomy 7/49	N.E.D.* 8 mos. 3/50
2. J. H. 63 M	0	Adenoca. gr. 2 nodes clear	Rectum	1937	A-P resection	10	Cough	Pap. V, x-ray	Sq. Ca. gr. 2	X-ray therapy 1948	D.O.D.† 1948
3. E. B. 58 F	0	Infiltrating Duct Ca.	Breast	1946	Rad. mastectomy	3	Chest pain	X-ray aspir. biopsy	Bronchiogenic epid. gr. 3 positive nodes	Pneumonectomy 8/49	D.O.D. 10/49
4. M. G. 56 F	0	Endomet. Ca.	Uterus	1943	Hysterectomy	3	Cough	X-ray, biopsy	Bronchiogenic Ca.	X-ray therapy 2/46	Died 7/46 cerebr. met.?
5. A. B. 71 M	0	Papillary epid. gr. 1	Bladder	1941	Resection	2	Hemoptysis	Biopsy	Bronchiogenic Ca. gr. 2	Radon applicator 12/42	Died uremia 12/43 12 mo.
6. C. G. 65 F	0	Lymphatic	Leucemia	1945	X-ray P-32	5	Cough	X-ray, Pap. V	Bronchiogenic Ca. Metastases to liver (autopsy)	X-ray 6/49	D.O.D. 3/50
7. M. McT. 52 F	0	Sq. Ca.	Buccal mucosa	1948	X-ray excision	1	Cough	X-ray, Pap. V	Sq. Ca. lung gr. 2 Pos. intrapulmonic node	Pneumonectomy 9/49	Evid. met. 3/50

8. R. K. 60 M	0	Basal cell	Skin	1948	X-ray	2	Cough	X-ray Pap. V	Bronchiogenic Ca.	X-ray 2/50	D.O.D. 4/50 2 mo.
9. S. C. 46 M	0	Basal cell	Skin	1927	Excision	8	Cough	X-ray biopsy	Epid. Ca. gr. 2	X-ray 10/36	D.O.D. 12/36 2 mo.
TRIPLE PRIMARY											
10. A. C. 40 F	0	1. Infiltr. Duct Ca. pos. nodes	Breast	5/41	Rad. mastectomy	8	Routine x-ray	X-ray Pap. III	Bronchiogenic Ca. bronchiolar type	11/49 R.U.L. and R.M.L. lobectomy	3/50 N.E.D. 4 mo.
		2. Adenoca. gr. 2 Duke's B	Sigmoid	9/49	Sigmoidectomy	2 mo.					
Synchronous Multiple Primaries											
11. W. B. 55 M	0	Sq. Ca. gr. 2	Palate	8/49	X-ray	0	Routine x-ray	X-ray Pap. V	Bronchiogenic adenoca. neg. nodes	9/49 Pneumonectomy	D.O.D. 2/50
12. J. G. 80 M	0	Epid. Ca. gr. 3	Intrinsic larynx	2/48	Laryngectomy	0	Routine x-ray	X-ray Pap. V	Epid. Ca. gr. 2	4/48 Intracavitary radium	N.E.D. 18 mo. 10/49
13. T. McC. 56 M	0	Epid. Ca. gr. 2 in situ	Intrinsic larynx	4/48	Partial laryngectomy	0	Cough and hemoptysis	Pap. V x-ray	Epid. Ca. gr. 3 positive nodes	5/48 R.U.L. and R.M.L. lobectomy	11/48 died ? chest neg.
14. R. McA. 68 M	0	Basal cell	Skin	8/48	Excision	0	Hemoptysis	Aspir. biopsy, x-ray, Pap. III	Epid. Ca. gr. 3	7/48 Pneumonectomy	3/50 N.E.D. 20 mo.
15. R. P. 65 M	0	Sq. Ca. gr. 1	Tongue	9/47	Glossectomy	0	Routine x-ray	Pap. V biopsy	Epid. Ca.	9/47 X-ray	D.O.D. 4/48 7 mo.
16. A. R. 63 M	0	Sq. Ca. gr. 2	Gingiva	9/41	X-ray	0	Routine x-ray	X-ray biopsy	Sq. Ca. gr. 2 of trachea	10/44 X-ray	D.O.D. 5/45 7 mo.

†Died of disease

*No evidence of disease.

TABLE III—CONT'D

FIRST PRIMARY							LUNG PRIMARY				
NAME AGE SEX	FAMILY HISTORY (CA.)	PATHOLOGY	SITE	YEAR TREATED	METHOD	TIME INTERVAL (YEARS)	FIRST SYMPTOM	DIAGNOSIS ESTABLISHED	PATHOLOGY	TREATMENT	FOLLOW-UP
17. G. K. 68 M	0	Sq. Ca. (Early)	Vocal cord	1/48	Cordectomy	0	Routine x-ray	X-ray Pap. V	Epid. Ca.	2/48 Thoracotomy and x-ray	D.O.D. 5/49 13 mo.
18. E. H. 56 M	0	Epid. Ca.	Renal pelvis	7/47	Nephrectomy	0	Hemoptysis	X-ray Pap. V	Epid. Ca. gr. 2 nodes clear	12/46 Pneumonectomy	D.O.D. 12/47 12 mo.
19. J. R. 65 M	0	Sq. Ca. gr. 2	Gingiva	10/39	X-ray	2 mo.	Cough	Biopsy	Epid. Ca.	8/40 X-ray	D.O.D. 9/40 1 mo.
20. L. B. 64 M	0	Sq. Ca. gr. 2	Larynx	5/49	Laryngectomy	0	Routine	X-ray Pap. III	Sq. Ca. gr. 2 nodes clear	3/49 Pneumonectomy	3/50 N.E.D. 12 mo.
21. J. H. 62 M	0	Basal cell	Skin axilla	12/43	Excision	0	Cough	X-ray node	Epid. Ca.	12/43 X-ray	3/44 D.O.D. 3 mo.
22. A. O. 70 M	0	Sq. Ca. gr. 2	Flr. of mouth	10/42	X-ray	0	Routine	X-ray biopsy	Epid. Ca.	11/42 X-ray	D.O.D. 12/42 1 mo.
23. R. L. 35 M	0	Ca.	Thyroid	9/43	Asp. mass	0	Chest pain	X-ray biopsy	Bronchiogenic Ca.	X-ray 9/43	D.O.D. 11/43 2 mo.
24. J. C. 65 M	0	Epid. Ca.	Tongue	1/46	X-ray	0	Cough	X-ray biopsy	Epid. Ca.	X-ray 2/46	D.O.D. 4/46 2 mo.
25. C. H. 77 M	0	Basal cell	Skin	8/47	X-ray	0	Chest pain	X-ray aspir. biopsy Pap. V	Epid. Ca.	X-ray 8/47	D.O.D. 12/47 4 mo.

Additional aid in diagnosing asymptomatic shadows may be derived from previous chest roentgenograms. Tomography will help to reveal bronchial changes in the absence of atelectasis, and, of course, serial roentgenograms will show changes and new lesions. A delay of even three weeks, however, waiting for a significant alteration on the appearance of a shadow or for a new metatasis may convert a resectable to a nonresectable lung cancer.

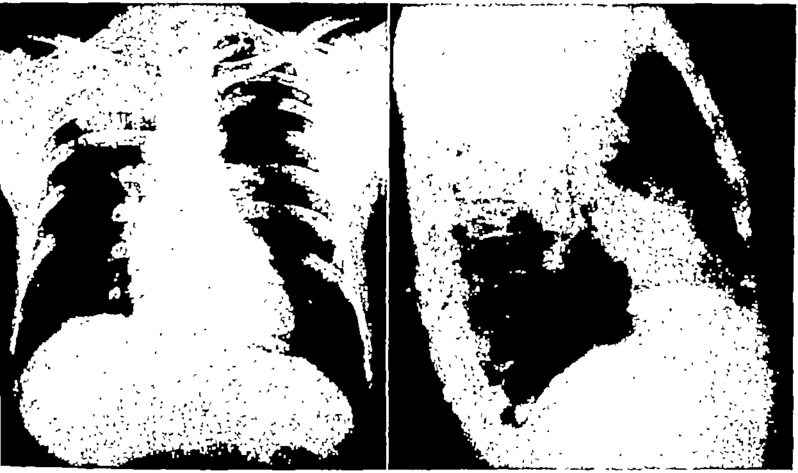

Fig. 2 (Case No. 11).—Posteroanterior and lateral chest roentgenograms, showing shadow and partial atelectasis of right upper lobe.

Bronchoscopy and Exfoliative Cytology.—Effler, Blades, and Marks[3] have stated that it is almost impossible to determine the exact nature of an asymptomatic lung tumor before it is excised. Nevertheless, in four cases, it was possible to make a presumptive preoperative diagnosis of primary lung cancer by obtaining histologic material that differed from the second cancer. In two cases (No. 2 and 11) this was accomplished by exfoliative cytological studies, stained according to the method of Papanicolaou; in another case (No. 4) by biopsy during bronchoscopy; and in still another (No. 3) by aspiration biopsy.

Sputum and bronchial washings stained for malignant cells in particular aid the diagnosis of peripheral lesions that are detected roentgenographically. These are usually early growths and are not accessible to bronchoscopic vision. In Case No. 2, a correct diagnosis was made when the first cancer was an adenocarcinoma of the rectum and the cytologic picture of the bronchial washings was squamous carcinoma. A total pneumonectomy was performed and the diagnosis of bronchiogenic carcinoma was confirmed.

Dr. Papanicolaou[3] states that in sputum or bronchial aspirate containing clusters of cells the varieties of primary lung cancer can often be distinguished. Approximately 85 per cent of all lung cancers can be diagnosed by cytology studies. On the other hand, metastases tend to yield scanty exfoliations and a lessened opportunity for cytologic diagnosis. Further studies are being made which may help to clarify this problem.

Biopsy at Operation.—In two cases (No. 10 and 20) final diagnosis was derived from the findings at exploratory thoracotomy. Under the equivocal circumstances that surround solitary lung lesions such as were found in these two patients, the lung is carefully examined at operation for signs of multiple parenchymal nodules which might indicate diffuse metastases not demonstrable by roentgenogram. If found, one can usually be excised for histologic examination.

Tumors located near the hilum and seeming to arise in the main-stem bronchus, as in Case No. 20, are considered to be primary lung cancers and a total pneumonectomy is performed for their removal. This provides the only means of securing a complete specimen for histologic study without incising the lesion itself, thereby running the risk of intrapleural dissemination of infection and/or neoplastic tissue.

The problem of distinguishing solitary peripheral lesions from metastasis at exploratory thoracotomy is more difficult. There were six instances (not recorded in this paper) in which metastasis in the lung was found, rather than a primary lung tumor. Various methods were employed in the operating room to help establish their identity so that the appropriate procedure could be performed. Aspiration biopsy of the tumor through the open chest provided tissue for a quick pathologic diagnosis and proved of value only when the histologic report of the primary lesion elsewhere was available for comparison. However, this procedure is now reserved for unresectable lesions, where a biopsy is of academic interest only.

Wedge and segmental resection of the smaller, more peripherally-placed lesions has been used, but it is felt that lobectomy affords a better chance of deciding whether the lesion is a primary tumor of the lung by permitting the study of its relationship to the bronchial tree. In addition, it is a safer procedure because it provides a wider and more complete excision of the tumor. If, upon gross examination of the specimen and the frozen section of the lesion, the presence of a primary lung cancer is established, a total pneumonectomy with hilar and mediastinal lymph node dissection can be performed, although in some clinics, a lobectomy is used as the complete procedure for the treatment of lung cancer confined to one lobe. Should the lesion prove to be a metastasis, nothing further need be done. Many of the thirty-five cases reported in the literature, in which metastatic foci were excised from the lung, obtained good palliation and surprisingly long survival rates.[1]

TREATMENT

Of the twenty-five lung cancers in this series, eleven were surgically explored—seven had pneumonectomies; two, lobectomies; and two were con-

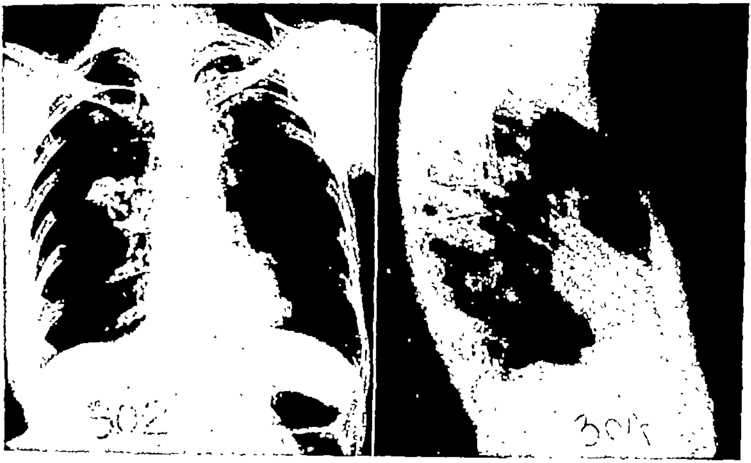

Fig. 3 (Case No. 10).—Triple primary, posteroanterior and lateral views. Chest roentgenograms showing opacity in right upper and middle lobes.

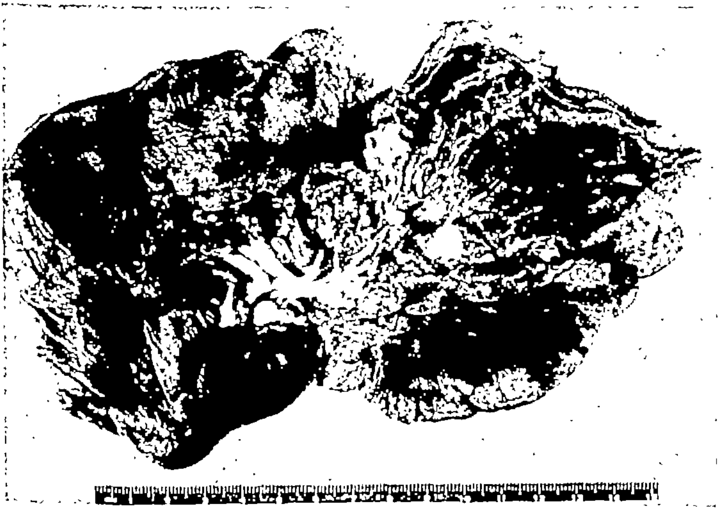

Fig. 4. (Case No. 10).—Triple primary. Right upper and middle lobes containing lesion.

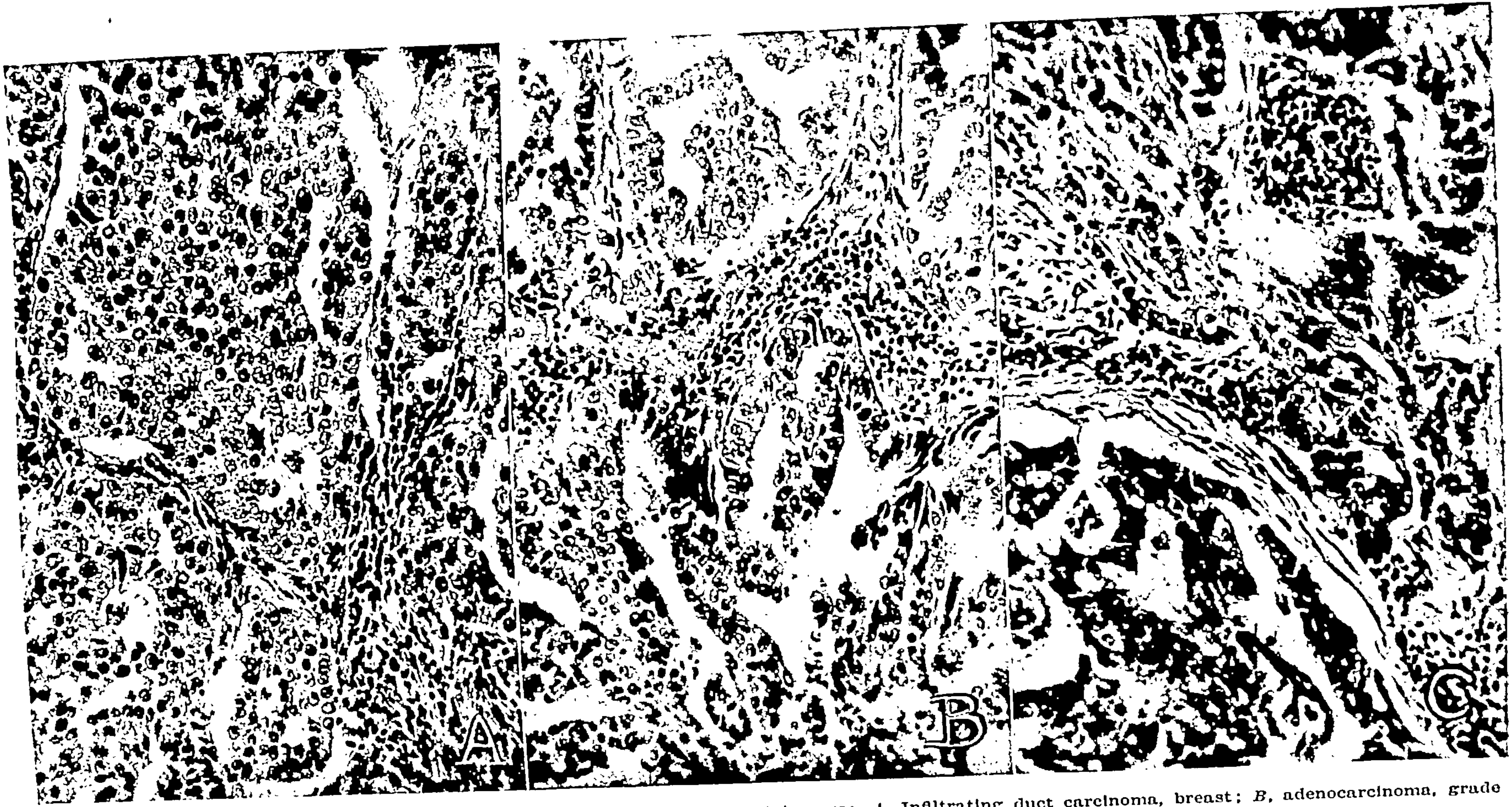

Fig. 5. (Case No. 10).—Photomicrographs of the triple primary malignant tumors: *A*, Infiltrating duct carcinoma, breast; *B*, adenocarcinoma, grade 2, of rectum; *C*, bronchiogenic carcinoma, bronchiolar type.

sidered nonresectable and were subsequently irradiated. It is worth noting that eight of these surgical procedures were performed in the last two years, which fact can be construed as an indication of a more aggressive surgical policy.

Of the nine patients who underwent surgical excision, four died of disease—two, six, eight, and twelve months after pneumonectomy. One patient (Case No. 7) is living six months postoperatively, although there are metastases in the remaining lung. The other four cases are living without evidence of disease—four, eight, twelve, and twenty months after operation—and include a patient with triple primary cancer (Case No. 10) who is living eight years after radical mastectomy, six months after sigmoidectomy, and four months after right upper and middle lobe lobectomy.

Twelve patients were treated only by irradiation and two others were added after exploratory thoracotomy revealed nonresectable lesions. Except for palliative benefits, roentgen-ray therapy was of little value in the prolongation of life, all of these patients dying of extension of the lung cancer within thirteen months of the institution of treatment.

Two cases received local irradiation by the application of intrabronchial, radon-containing, capsules through the bronchoscope. Case No. 5 survived twenty-four months and died of uremia, secondary to the extension of the bladder carcinoma. Chest roentgenogram, taken just prior to death, was reported as negative. One patient, Case No. 12, is alive at present without evidence of extension of the primary carcinomas of the lung and intrinsic larynx, eighteen months after treatment.

Two cases will be described in some detail.

CASE No. 1.—This patient was a 54-year-old white man who first came to Memorial Hospital on July 19, 1940, with a complaint of rectal bleeding of eight months' duration. Biopsy of a rectosigmoid lesion, 12.5 cm. from the anal margin, was reported to be adenocarcinoma, grade 2. *On Oct. 24, 1940, a one-stage, combined abdominoperineal resection* was performed. On subsequent follow-up visits, the patient was reported to be well, until May 2, 1949, when he complained of slight cough and bloody sputum. Roentgenogram of the chest indicated the possibility of an early bronchiogenic carcinoma. Bronchoscopy had revealed no apparent abnormality. Papanicolaou studies of bronchial washings were reported as Class V, "Conclusive evidence of a squamous carcinoma of the lung." On July 15, 1949, at exploratory thoracotomy, a tumor mass was found in the apex of the left lower lobe, measuring about 4 cm. in diameter, and extending across the interlobar fissure to the left upper lobe. A left pneumonectomy was done and the specimen was reported as bronchiogenic squamous carcinoma—nodes clear. The patient had an uneventful recovery and was without evidence of disease eight months later.

Comment.—The development of metachronous lesions, in this case of the rectum and lung, was separated by nine years, and a preoperative diagnosis of a new primary pulmonary cancer was derived from roentgenograms and bronchial cytologic studies.

CASE No. 6.—The patient was a 65-year-old white woman, who was first seen on Sept. 29, 1948, presenting a history of lymphatic leucemia of five years' duration. She had been treated elsewhere for the disease by roentgen irradiation, radioactive phosphorus, and urethane. On examination, there was generalized adenopathy and hepatosplenomegaly. White blood count was over 200,000, with 92 per cent lymphocytes. She had no pulmonary complaints, but a submitted chest roentgenogram taken four months previously showed a 6 cm. opacity in the right lower lung field. This was reported by the radiologist as "consistent with bronchiogenic carcinoma." Bronchoscopy did not visualize the tumor. A sputum specimen was reported as Class V, "Shows large masses of lymphocytes and also clusters of neoplastic cells suggestive of a malignant lung tumor, adenocarcinoma in type." Roentgen-ray therapy to the lung lesion was begun on May 6, 1949, and the patient was given 3,000r. to each of two chest portals, anterior and posterior, using the 1,000 KV. machine. She remained asymptomatic until Feb. 9, 1950, when she complained of marked weakness, nasal hemorrhages, and she developed axillary and inguinal lymph node enlargement. ACTH was administered without avail. She died on March 20, 1950. At autopsy, the diagnosis of terminal alveolar adenocarcinoma of the right lower lobe of the lung, metastatic to liver, was revealed, together with diffuse evidences of lymphatic leucemia.

Comment.—In this instance, radiation therapy was selected as the method of choice because the hemorrhagic propensity of patients with leucemia precluded surgical intervention.

SUMMARY

1. In 1,493 cases of lung cancer at Memorial Hospital, there were twenty-five multiple primary cancers in which the lung was the site of one of the tumors.
2. There were fifteen instances of synchronous and nine of metachronous multiple cancers. One triple primary cancer of the breast, rectum, and lung is included.
3. The relative importance of the methods of establishing a definite diagnosis of the pulmonary lesion has been discussed. The value of routine chest roentgenograms and of exfoliative cytologic studies of bronchial secretions has been emphasized.
4. Radiation therapy has value as a palliative measure in the treatment of the cancer, primary in the lung, but surgical intervention may be preferable, for it serves both as a diagnostic and therapeutic measure.
5. There should be no defeatism engendered by the appearance of a lung shadow in the presence of a known cancer at another site. Rather, aggressive measures directed at establishing the nature of the new growth and eradicating it must be instituted.

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(See discussion on page 358.)

THE SURGICAL MANAGEMENT OF CARCINOMA OF THE LUNG

A STUDY OF THE CASES TREATED AT THE MASSACHUSETTS GENERAL HOSPITAL FROM 1930 TO 1950

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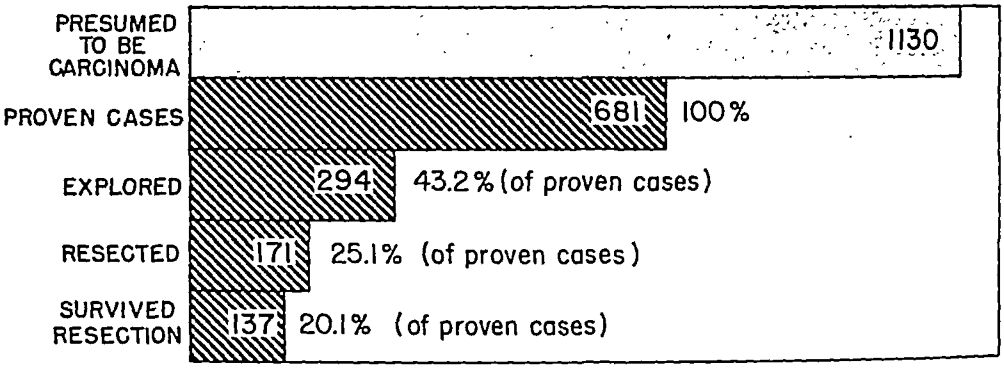
DURING the twenty-year period, 1930 to 1950, a clinical diagnosis of carcinoma of the lung was made in 1,130 patients at the Massachusetts General Hospital. In 681 of these, the presumptive diagnosis was confirmed by histologic evidence obtained by study of the surgical specimen, autopsy, or by biopsy of the original tumor or its metastases. Sarcoma, metastatic carcinoma, and other tumors of the lung have been excluded from the present study. Of these 681 proved cases, 294 patients were subjected to thoracotomy (Fig. 1) and a lobectomy or pneumonectomy carried out in 171 (25.1 per cent of proved cases, 58.2 per cent of those explored). One hundred and thirty-seven survived resection and left the hospital alive, 20.1 per cent of the patients in whom the diagnosis was established histologically. In order to avoid diagnostic error which could affect survival figures, the microscopic sections of the resected tumors have been reviewed with a pathologist and tumors of uncertain origin or cell characteristics excluded. Adenoma of the bronchus has been recognized as a separate entity and has not been included in the figures presented above. This has been done because, regardless of any controversy concerning its cell characteristics, its clinical behavior is such as to warrant separate consideration particularly in the light of survival rates after resection.

The patients who form the basis of this report include all those admitted to the medical and surgical services of the general hospital in whom the diagnosis was made, as well as those individuals referred to the private divisions of the hospital. In the majority, the diagnosis had not been established prior to admission. In histology, age, and sex distribution, they conform to the pattern of the disease that has been previously recorded in the literature. The follow-up on all who underwent resection before January, 1948—that is, at least two years prior to this study—is complete. Thus all figures relating to survival are based on a 100 per cent follow-up—a matter of basic importance in cancer statistics. The number of operations and hospital mortality for the years 1948 and 1949 have been added to round out the over-all picture for the twenty-year period. The patients treated in those two years have not been considered in the calculations of survival, but are inserted to characterize the present management of carcinoma of the lung better than the series extending back to 1930.

Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 16-18, 1950.

SELECTION OF OPERATION

In the twenty-year period, 1930 to 1950, 114 pneumonectomies and 57 lobectomies were performed for primary carcinoma of the lung. These operations were carried out on the basis of one of two fundamental assumptions. The first was that the disease was a localized process and therefore might be eradicated by surgical extirpation; the second, that the removal of a whole lung or one of its lobes might alleviate the suffering arising from pain, hemorrhage, or suppuration in uncontrollable cancer and thus make a limited period of survival more worth while.



PRIMARY CARCINOMA OF THE LUNG OVER A 20 YEAR PERIOD
1930 to 1950

Fig. 1.

Both operative mortality and survival rates have been calculated for the entire series without the usual attempt to correct for those resections undertaken when it may have been the estimate of the operator that the disease had exended beyond the limits of extirpation. In this as in all series of operations for cancer, many patients have been benefited even though they have ultimately died of the disease. It may be assumed, however, that resections undertaken for "palliation" only were evenly distributed between the lobectomy and pneumonectomy groups.

When resection is carried out under the first assumption, however, with full hope of eradicating what is believed to be a localized disease, the important question is whether significantly better results can be achieved if the entire organ is removed. The survival figures shown throw some light on this point. It should be understood that lobectomy has been carried out not merely as a local excision of a primary growth, but as a complete dissection of an anatomic unit of the lung to include the adjacent lymph nodes. There can be *no difference of opinion as to the type of operation* to be performed under circumstances that require a pneumonectomy for complete excision of a primary growth or grossly identified secondary deposits.

Lobectomy, with removal of all gross evidence of the disease, has been considered reasonable under the following conditions: (1) when there was evidence of diminished pulmonary or cardiac reserve; (2) when uncertainty of diagnosis existed and the lesion in question could be totally excised by lobectomy; (3) when the lesion was small, peripheral, and without evidence of lymph node extension; (4) when the carcinoma had extended beyond surgical bounds, but when the bulk of primary tumor could be removed by lobectomy with the hope of relieving symptoms.

The patient's pulmonary reserve has been appraised upon clinical grounds rather than upon formal pulmonary "function" tests. Emphysema, pulmonary fibrosis, previous pulmonary disease, and old injuries to the chest wall have been taken into account and ability to perform the usual daily tasks without unusual dyspnea taken as the measure of exercise tolerance. The apparent rather than the actual age of the patient has been a part of our estimate of pulmonary reserve. Diminished cardiac reserve has been assumed if there was a history of congestive failure, angina pectoris, hypertension, or arteriosclerosis, especially when supported by evidence of coronary insufficiency or past myocardial infarction in the electrocardiogram or by cardiac enlargement and tortuosity of the great vessels in the roentgenographic examination of the chest.

Uncertainty of diagnosis has led to the employment of lobectomy as a means of establishing the presence of malignant disease before accepting the commitment to total pneumonectomy. If the diagnosis of cancer was confirmed and the resected lymph nodes proved uninvolved, the question then arose as to the need to extend a lobectomy to a pneumonectomy. At this point the operator has been guided by what in his judgment constituted a reasonable effort to eradicate the disease by extirpation balanced against the status of the patient, particularly with respect to his cardiorespiratory function. Lobectomy is not merely a local resection of the primary growth. As performed in our hands it has included not only the lymph nodes at the level of the lobar bronchus, but also mediastinal nodes. For example, a right upper lobectomy should include the division of the azygos vein and removal of the paratracheal nodes as well as those lying superior to the right pulmonary artery anterior to the trachea. It has sometimes included resection of the right middle lobe with resection of the nodes lying below the middle lobe bronchus.

Small peripheral tumors with grossly negative lymph nodes have often been treated by lobectomy. The increasing frequency of these tumors that results from earlier diagnosis of the disease introduces a very serious question as to whether wide excision of apparently normal lung tissue is as vital to the life of the patient as the maximum preservation of his pulmonary reserve.

Last, some lobectomies have been performed for severe hemorrhage, pain secondary to chest wall invasion, or localized infection arising from a tumor primary in that lobe, even though there were widespread metastases.

In each patient the decision as to the type of resection has been based upon a number of considerations that apply to the individual concerned rather than upon arbitrary rules drawn up without regard to their applicability to the problem at hand.

With this statement of general policy in the management of cancer of the lung, we present the results of pneumonectomy and lobectomy at the Massachusetts General Hospital from 1930 to the present.

OPERATIVE MORTALITY

Among 294 patients who were explored, 171 (58.2 per cent) had resections (25.1 per cent of all proved cases). The first lobectomy for carcinoma in this series was performed in 1930,* the first pneumonectomy in 1933.† Among those who had exploratory thoracotomies only, the mortality was 10.6 per cent. Of 114 patients who underwent pneumonectomy, there were 26 hospital deaths in the years 1933 to 1950, an operative mortality of 22.8 per cent. Of 57 patients treated by lobectomy from 1930 to 1950, there were 8 deaths, an operative mortality of 14 per cent (Fig. 2). Although this means a higher hospital survival rate for the smaller series of cases treated by lobectomy, it should be noted that many of the patients who died following pneumonectomy could not have had complete extirpation of their disease by less radical surgery so that the procedure was indicated in the face of added risk. The ages of the patients who had pneumonectomies are much the same as those who had lobectomies, both as to average age and maximum age. These figures have been plotted in Fig. 3.

The operative mortality rates computed for a series extending back to 1930 are chiefly of historical interest. A more accurate picture of the immediate status of pulmonary resection for cancer is given by our experience in the years 1948 and 1949. In these years was felt the full effect of present-day measures to combat infection, replace blood loss, and deal with cardio-respiratory problems, but, more important, the encouraging evidence that these patients were coming to surgery earlier in their disease. For comparison, therefore, in Fig. 2 the mortality rates are divided into resections performed before 1948 and those performed in 1948 and 1949. Among 87 pneumonectomies in the years 1933 through 1947 there were 25 deaths, an operative mortality of 28.7 per cent compared with one death following 27 pneumonectomies in 1948 and 1949, an operative mortality of 3.7 per cent. After 31 lobectomies in the years 1930 through 1947, there were 7 deaths, an operative mortality of 22.6 per cent compared with 1 death following lobectomy in 26 patients in the years 1948 and 1949, an operative mortality of 3.8 per cent. The equality of distribution between the two types of resection in 1948 and 1949 is worthy of note.

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*The lobectomies in this series include the early cases reported in 1933 (J. THORACIC SURG. 2: 254). In the first lobectomy performed on Oct. 30, 1930, the carcinoma was too close to the hilum to permit the use of the tourniquet technique then in common usage. Individual ligation of the lobar artery and vein was followed by transection of the lobar bronchus. Because Sauerbruch had reported several deaths from mediastinal emphysema following primary closure of a large bronchus at the hilum, a tube was sutured to the bronchial stump and brought to the outside of the chest wall. The patient died of pneumonia.

The patient recorded as Case 4 in the above-mentioned article is still living. Her tumor was later classified as an adenoma. The lower and middle lobes were removed on Aug. 10, 1931, by intrahilar dissection and the intermediate bronchus closed by primary suture.

†The first pneumonectomy of this series was a single stage resection of the right lung and a portion of the diaphragm for adenocarcinoma performed on Nov. 9, 1933. The patient (M.G.H., No. 332942) was discharged ambulatory on December 9 and returned to her home. She was readmitted on December 15 and died on Dec. 24, 1933. Autopsy showed sound healing of the operation site but widely disseminated metastic carcinoma.

In Overholt's case (J. THORACIC SURG. 4: 196, 1934), repeatedly referred to as the "first single stage right pneumonectomy," the date of operation is recorded as 11 days after November 2 (Nov. 13, 1933). The patient is reported as surviving and it has been stated that the tumor was subsequently reclassified as bronchial adenoma.

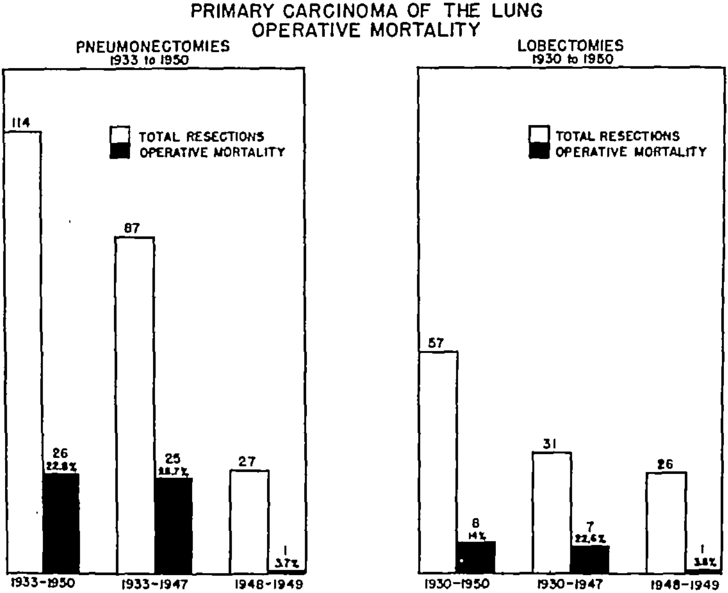

PRIMARY CARCINOMA OF THE LUNG
OPERATIVE MORTALITY
PNEUMONECTOMIES
1933 to 1950
TOTAL RESECTIONS
OPERATIVE MORTALITY
114
26
22.8%
87
25
28.7%
27
1
3.7%
1933-1950
1933-1947
1948-1949
LOBECTOMIES
1930 to 1950
TOTAL RESECTIONS
OPERATIVE MORTALITY
57
8
14%
31
7
22.6%
26
1
3.8%
1930-1950
1930-1947
1948-1949

FIG. 2.

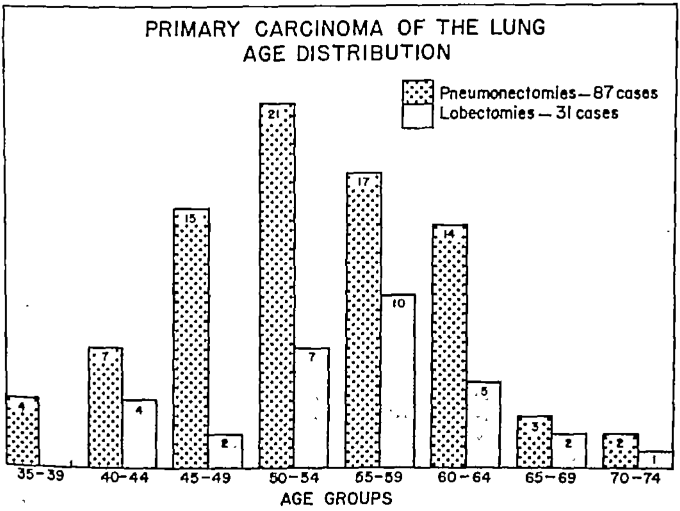

PRIMARY CARCINOMA OF THE LUNG
AGE DISTRIBUTION
Pneumonectomies — 87 cases
Lobectomies — 31 cases
4
7
4
15
2
21
7
17
10
14
5
3
2
2
1
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
AGE GROUPS

FIG. 3.

The effect of chest surveys in adding early tumors among favorable subjects for surgery is important. The increasing awareness of doctors and patients alike to the necessity for chest x-ray examinations followed by diagnostic studies for abnormal lung shadows has enabled more patients to be operated upon while their tumors were still in a stage amenable to resection.

SURVIVAL

The survival rates for patients treated by resection is presented in the following ways: (1) percentage of five-year survival among patients operated upon five or more years ago; (2) percentage survival by six-month periods up to five years of all patients who underwent resection. The number of patients entering into this calculation diminishes, of course, after three years as those cases done less than three to five years before are excluded; (3) percentage survival also by six-month periods up to five years of patients who left the hospital alive after operation; (4) percentage survival by six-month intervals of all patients who underwent resection, either lobectomy or pneumonectomy, classified according to the presence or absence of lymph node involvement noted in pathologic examination of the resected specimen; and finally (5) the number of patients at present surviving among all individuals who have undergone resection.

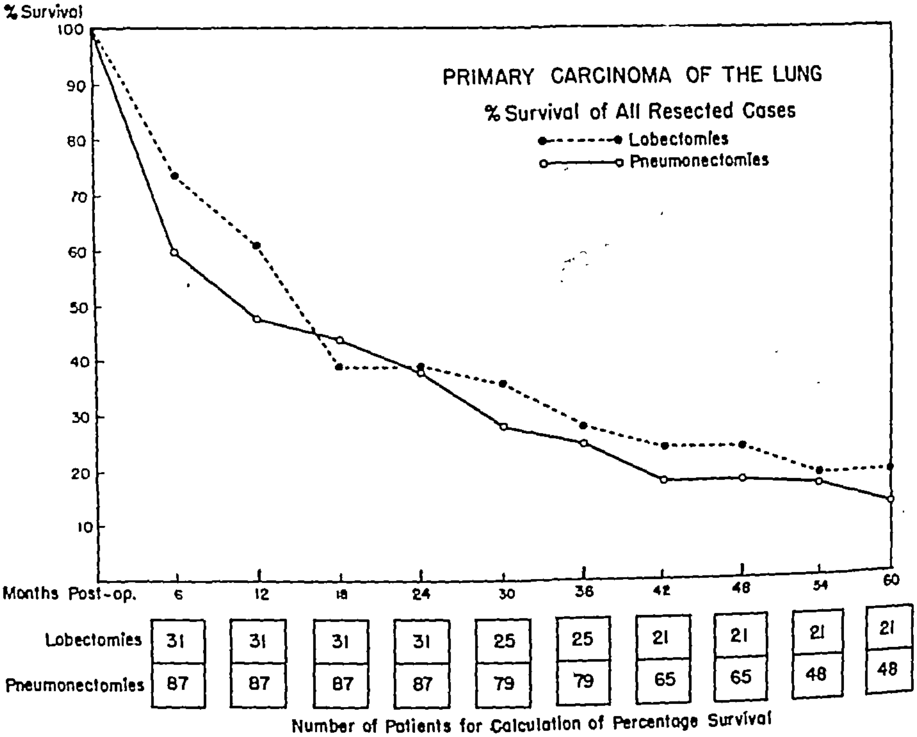
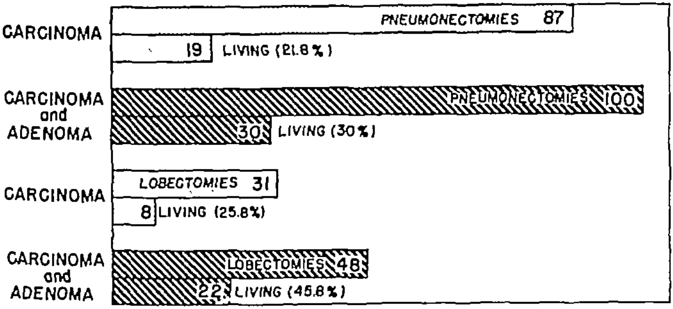


Fig. 4.

There were 48 patients who had a pneumonectomy five or more years ago and of these, 6, or 12 per cent, survived five or more years. Similarly, there were 21 patients treated by lobectomy five or more years ago, 4, or 19 per cent, survived five or more years (Fig. 4).

It is instructive to add the 17 lobectomies and 13 pneumonectomies that were done for adenoma to the group of patients in whom these procedures were carried out for carcinoma. Among the patients with adenoma, there were two hospital deaths, none later than 1936. There were 3 patients who died a year or more after leaving the hospital, all 3 of other diseases, none of whom had evidence of recurrence or distant metastases at autopsy. Added to the carcinomas they make a total of 100 pneumonectomies and 48 lobectomies performed before 1948. The two-year survival rates, including hospital mortality, are charted in Fig. 5. They raise the survival for all cases followed at least two years for pneumonectomy from 22 to 30 per cent and for lobectomy from 26 to 46 per cent.

Returning to the problem of carcinoma of the lung exclusive of adenoma, if one considers percentage survival by six-month periods up to five years, the curves for lobectomies and pneumonectomies are also in close agreement, either according to patients who left the hospital and therefore had an opportunity to survive, or according to the total number of patients undergoing resection. Among the latter, the increased hospital mortality in the pneumonectomy group during the period 1930 to 1947 increases slightly the margin in favor of lobectomy.



Effect on Survival of adding Adenoma to Carcinoma
Cases operated on 2 or more years; 1930 to 1948, followed into 1950
(Includes hospital mortality)

FIG. 5.

The rate of survival for those who left the hospital alive after resection for primary carcinoma has been charted in Fig. 6. It shows a five-year survival rate of 20 per cent for the pneumonectomies (6 patients surviving five or more years), and a 25 per cent for lobectomies (4 patients surviving five or more years).

As might be predicted, the presence of involved lymph nodes in the operative specimen decreased the long term chances of survival of the patients who left the hospital alive. These figures are graphically presented in Fig. 7. Of 29 patients with negative nodes, 10, or 34 per cent, survived five years, and

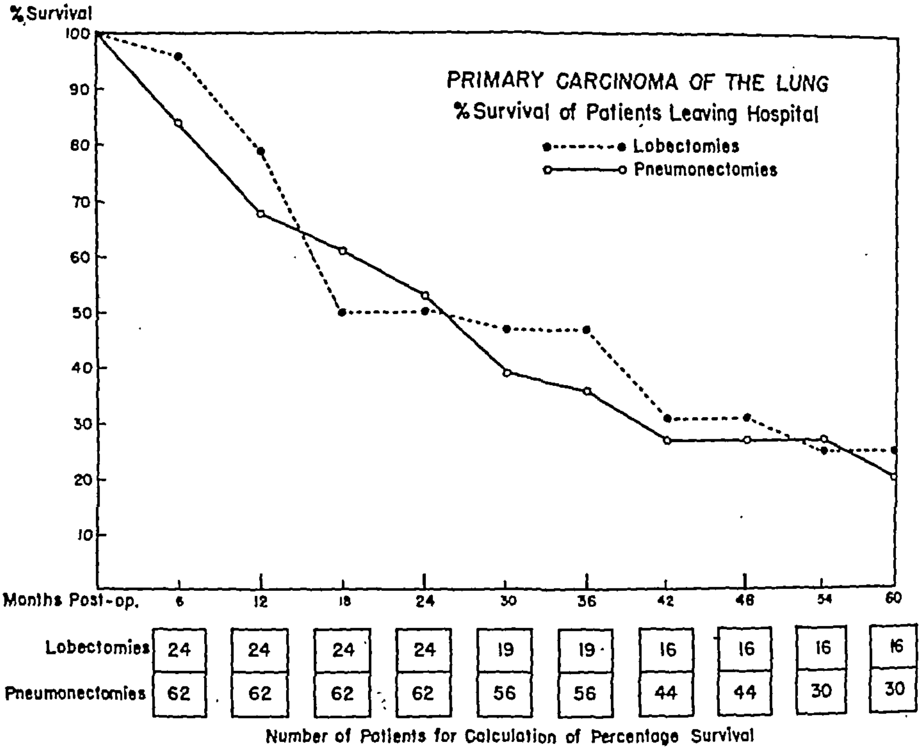

% Survival
100
90
80
70
60
50
40
30
20
10
PRIMARY CARCINOMA OF THE LUNG
% Survival of Patients Leaving Hospital
Lobectomies
Pneumonectomies
Months Post-op.
6
12
18
24
30
36
42
48
54
60
Lobectomies 24 24 24 24 19 19 16 16 16 16
Pneumonectomies 62 62 62 62 56 56 44 44 30 30
Number of Patients for Calculation of Percentage Survival

Fig. 6.

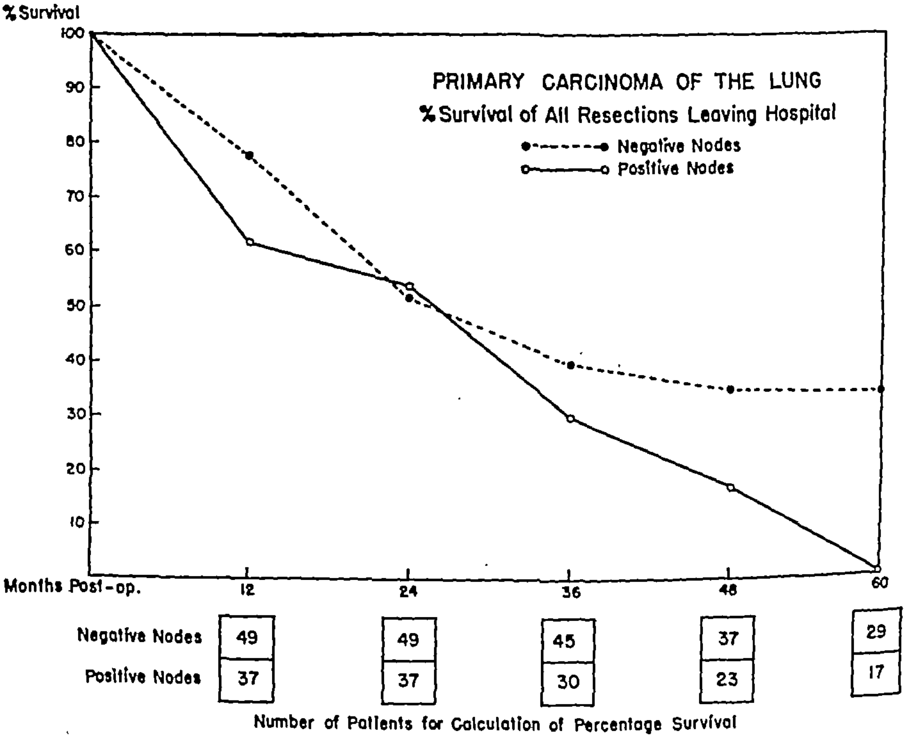
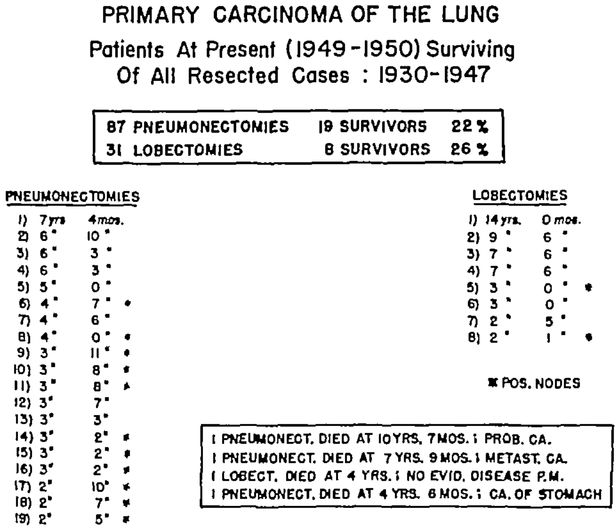

% Survival
100
90
80
70
60
50
40
30
20
10
PRIMARY CARCINOMA OF THE LUNG
% Survival of All Resections Leaving Hospital
Negative Nodes
Positive Nodes
Months Post-op.
12
24
36
48
60
Negative Nodes 49 49 45 37 29
Positive Nodes 37 37 30 23 17
Number of Patients for Calculation of Percentage Survival

Fig. 7.

there was no survivor at five years among those with positive nodes. Only patients operated upon five or more years ago are considered. Of the patients operated upon within five years there are 2 with positive nodes who are still alive more than four years after operation.

Considering the survival of patients on an individual basis, 4 of the patients who had pneumonectomies are alive and well over six years after operation. Four of those who had lobectomies are alive and well seven years or more postoperatively, 1 having survived for fourteen years. Among those who survived pneumonectomy there are 3 who died at four and one-half, seven and one-half, and ten and one-half years, respectively. One died at four and one-half years of carcinoma of the stomach, and the other two presumably of recurrence of their disease. One patient died four years after lobectomy and at autopsy no evidence of recurrent disease was found.



PRIMARY CARCINOMA OF THE LUNG

Patients At Present (1949-1950) Surviving
Of All Resected Cases : 1930-1947

87 PNEUMONECTOMIES	19 SURVIVORS	22 %
31 LOBECTOMIES	8 SURVIVORS	26 %

PNEUMONECTOMIES

1)	7 yrs	4 mos.	
2)	6 "	10 "	
3)	6 "	3 "	
4)	6 "	3 "	
5)	5 "	0 "	
6)	4 "	7 "	*
7)	4 "	6 "	
8)	4 "	0 "	*
9)	3 "	11 "	*
10)	3 "	8 "	*
11)	3 "	8 "	*
12)	3 "	7 "	
13)	3 "	3 "	
14)	3 "	2 "	*
15)	3 "	2 "	*
16)	3 "	2 "	*
17)	2 "	10 "	*
18)	2 "	7 "	*
19)	2 "	5 "	*

LOBECTOMIES

1)	14 yrs.	0 mos.	
2)	9 "	6 "	
3)	7 "	6 "	
4)	7 "	6 "	
5)	3 "	0 "	*
6)	3 "	0 "	
7)	2 "	5 "	
8)	2 "	1 "	*

* POS. NODES

1 PNEUMONECT. DIED AT 10 YRS. 7 MOS.; PROB. CA.
1 PNEUMONECT. DIED AT 7 YRS. 9 MOS.; METAST. CA.
1 LOBECT. DIED AT 4 YRS.; NO EVID. DISEASE P.M.
1 PNEUMONECT. DIED AT 4 YRS. 6 MOS.; CA. OF STOMACH

Fig. 8.

At the present time, of the 87 patients who underwent total pneumonectomy before 1948, 19, or 22 per cent, survive. Of the 31 patients who underwent lobectomy in the same period, 8, or 26 per cent, are now alive, and so far as we are aware, free of disease (Fig. 8).

SUMMARY

1. The total experience with proved cases of primary carcinoma of the lung at the Massachusetts General Hospital for the twenty-year period, 1930 to 1950, has been presented.

2. The conditions under which lobectomy has been carried out in the treatment of cancer of the lung are reviewed.

3. Operative mortality statistics for lobectomy and pneumonectomy for the twenty-year period and for the last two years separately have been noted. In the past two years the operative mortality for both pneumonectomy and lobectomy has been less than 4 per cent.

4. The follow-up on the 87 pneumonectomies and 31 lobectomies performed before 1948 is complete. There is remarkably close agreement in survival rates for the two procedures.

5. As might be predicted, the presence of involved lymph nodes in the resected specimen has greatly diminished the patient's chance of long-term survival.

DISCUSSION ON "MULTIPLE CANCERS: PRIMARY IN THE LUNG AND OTHER SITES" BY DR. WILLIAM G. CAHAN, DR. FRANK S. BUTLER, DR. WILLIAM L. WATSON, AND DR. JOHN L. POOL;* AND "THE SURGICAL MANAGEMENT OF CARCINOMA OF THE LUNG" BY DR. EDWARD D. CHURCHILL, DR. RICHARD H. SWEET, DR. LAMAR SOUTTER, AND DR. J. GORDON SCANNELL

DR. ARTHUR H. AUFSES, New York.—It is interesting to hear Dr. Cahan and his associates present the results of their resection therapy in carcinoma of the lung, including a large number of lobectomies. When Dr. Harold Neuhof and I presented a paper before this Association in 1947, suggesting that lobectomy might be an adequate operation in certain types of carcinoma of the lung, it aroused considerable discussion, most of which was adverse. For that reason I should like to show two slides, one of which shows the results at Mt. Sinai Hospital in patients who survived operation over a period of 13 years from 1935 to 1947, inclusive.

(Slide.) Eighty-six patients survived operation; of the 86, 52 had pneumonectomies and 34 lobectomies. At the present date, 17 patients who had pneumonectomy are alive and well or considered cured, and 13 who had lobectomy, alive and well or considered cured. By cured, we mean that a few have since died but we have post-mortem evidence that they died of coronary or other diseases four or more years after operation, and at post mortem no evidence of the original carcinoma was found in the body. No patient who died within four years of operation is included in this group as considered cured. As you see, of 34 lobectomies, 13 are alive and well, 38 per cent. In the early years that we performed this operation there were four patients upon whom we performed lobectomies who would not meet our criteria today; if they were omitted from this series the percentage of survivals would be 43 per cent. Incidentally, of the 17 pneumonectomies, 7 are alive after more than five years, and, of the 13 lobectomies, 8 are alive for more than five years. So that we have a rather high percentage of lobectomies alive in comparison with the pneumonectomies. We believe that the patients with lobectomy will hold up.

(Slide.) We reviewed 849 carcinomas of the lung seen at Mt. Sinai Hospital over the same thirteen-year period and grouped them according to the length of time that they had symptoms—one month, two months, three months, four to six months, seven to twelve months, one to two years, and longer. If we take the survival rate in the various "duration of symptoms periods," we see that in the one-, two- and three-month periods the survival rate is only 2.8 per cent; in the six-month period it is 3.5 per cent; and in the one-year period 3.9 per cent. If we take the cases who had a longer history, more than one year, we have the remarkable figure of 3.9 per cent survival rate, which would seem to indicate that there are really two types of tumors: (1) the slow-growing type, the type one sees on the x-ray on routine examination, without symptoms, a small peripheral tumor. We feel that if no involved lymph nodes are found at operation, this type is a subject for lobectomy. (2) The main bronchus, rapid-growing and spreading lesion which gives early symptoms.

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*See page 335 for article by Cahan, Butler, Watson, and Pool.

DR. T. R. HUDSON, *Chicago.—At Hines Veterans Administration Hospital and* Wesley Memorial Hospital in Chicago we are currently engaged in a study of 150 cases of patients subjected to surgical treatment for carcinoma of the lung. The study is incomplete but at present we have been able to follow and have statistics on 114; 83 of those patients had pneumonectomy and, of the 83, 15 are alive today, an 18 per cent survival rate. Thirty-one patients had lobectomy and, of the 31, 8 are alive today—25 per cent survival. The earliest lobectomy was done 18 months ago and the oldest one 13 years ago, in 1937. This patient had a right lower lobe removed, also a number of ribs and a portion of the diaphragm because of local invasion. The mortality figures on the lobectomy are one death in 31 cases; for the pneumonectomies the figure was 4.5 per cent. That does not include any cases prior to 1943.

DR. EVARTS A. GRAHAM, St. Louis.—I am sure everyone has enjoyed these two interesting and important papers on this very important subject of bronchiogenic carcinoma. It seems to me that the results given by Dr. Soutter, from Dr. Churchill's and Dr. Sweet's clinic, show conclusively that patients will survive a five-year period after lobectomy in some instances. I think, however, that we should distinguish between what might be considered the ideal operation for cancer—and cancer is about the same whether in the lung or elsewhere—and one which theoretically is not ideal but will sometimes work. The statistics reported today are, I would say, of no significance except that they indicate that some patients will survive a five-year period after lobectomy. One cannot draw any conclusions *from a small number of cases, less than several thousand, I would say, about which* operation is the best so far as giving a high percentage of five-year survival rates. I think we are likely to be misled, perhaps, by the presentation of statistics which, because of the small number, do not really have much significance. There are not available at the present time a sufficiently large number of patients who have been operated upon for bronchiogenic carcinoma, to have statistically significant figures on end results.

I am glad, however, to have this subject brought up. There is no doubt, as everyone who has had experience in dealing with this disease realizes full well, that there are cases in which it is worth while to take a chance on a lobectomy because of the horrible situation in which the patient may be left if total pneumonectomy is performed. After all, a bad respiratory cripple is a very pathetic figure, and it is questionable whether we have done an act of kindness to some of those people by permitting them to live for more than five years, we will say, in this pathetic condition. It might be far better to take a chance with lobectomy in such a case and make the patient less of a respiratory cripple than he would be by perhaps doing a better theoretical operation—a total pneumonectomy—but leaving him so uncomfortable that life is hardly worth while for him.

I am rather surprised, in the series just quoted from Boston, that they have no successful results in cases with involved glands. In a series we studied of more than five-year survivals prior to 1947, we had three patients who had survived more than five years who had had involved glands. As a matter of fact, the Pittsburgh doctor who was my first patient for pneumonectomy showed, when his lung was re-examined many years later, that he had two involved glands invaded by carcinoma. He has passed his seventeenth year and is now in his eighteenth year, well, and still practicing obstetrics. We have had two other patients with involved glands who have survived more than five years.

There is one other point on which I want to "stick out my neck;" if there are any pathologists here perhaps they would like to say something on this to put me in my proper place. That is—and I just venture to put this proposition to you—that I think that before many more years have passed, you will all agree that many times the so-called adenocarcinoma arises in what is sometimes spoken of as the bronchial adenoma. Therefore, when one makes rigid distinctions in saying that he is dealing with and discussing adenocarcinoma, but is not saying anything at all about adenoma, I think he is making a mistake.

DR. M. E. DE BAKEY, Houston.—It is gratifying to observe the rather good results obtained by Dr. Churchill and his associates following lobectomy in carcinoma of the lung. I would add, however, that I am not particularly surprised at these results, because the mere fact that a lobectomy was done in these patients is, I think, a selective factor which tends to screen out the more advanced case. We know that there are a number of factors that affect the survival rate following resection in carcinoma of the lung. We have attempted to ascertain some of these factors by an analysis of our experience. On the basis of this analysis it was found that the most significant of all factors affecting prognosis is whether or not the lesion is still confined to the lung. The fact that lobectomy could be done in the cases just presented is an indication that the lesion was still localized within the lobe, and consequently had not extended beyond the borders of the lung. There is, of course, the possibility that in a certain number of the cases the disease may have extended by way of the lymphatics to the mediastinal nodes which may not have been reached by lobectomy, but certainly a fair proportion of the total number of patients in whom lobectomy was done would be those in which there was no extrapulmonary extension of the lesion. The significance of this factor, that is, the status of the growth at the time of operation, is well demonstrated in our pneumonectomy series by analysis of the cases into two groups; first, those in which the lesion was still confined to the lung and, second, those in which the lesion had already extended beyond the borders of the lung, either by extension of the disease grossly to the adjacent structures or to the regional lymph nodes. The difference in the five-year survival rates between these two groups was quite significant, the figures being respectively about 40 per cent and 12.5 per cent.

It is my impression that the purpose of this study by Dr. Churchill and his associates is not to determine whether lobectomy or pneumonectomy is the procedure of choice in carcinoma of the lung, but rather to learn if lobectomy under certain conditions would provide equally satisfactory results. Certainly, this is highly desirable information. As Dr. Graham has said, most of us have had experience with patients in whom we have felt that lobectomy might be a less risky and, under the circumstances, the preferable procedure. This presentation provides additional support for that belief. The indications given by Dr. Soutter showed that they have used this procedure, not as the procedure of choice for all cases of carcinoma of the lung, but rather as the procedure of choice in a given set of circumstances. I think this is an important point to keep in mind.

Finally, I would like to merely mention the fact, in support again of what Dr. Graham has said about not drawing definitive conclusions from statistics of this kind, that there are a number of factors in addition to the status of the growth which I have already mentioned that can influence the results in any given series, particularly in a relatively small series. I do not think we have yet acquired sufficiently large series to permit disregard of these variables in the statistical analysis. For example, the results can be greatly influenced by the number of private cases and the number of charity cases in the series. In our experience, the resectability rate was some three or four times greater among private cases than among the charity cases; this simply means that the former type of patient will have the less advanced and more likely curable lesion. Still another factor is the histologic type and grade of the growth. Thus it has been found that the most favorable survival rate occurred in patients with epidermoid carcinoma, and the poorest in those with undifferentiated carcinoma, and in both forms there was a progressive rise in fatality rates from Grade I to Grade IV. It is thus apparent that these and other variables and their relative weight in any series of cases may have an important bearing upon the results of an analysis.

DR. ARTHUR H. AUFSES, New York.—As you know, Dr. Neuhof and I have been attempting to make a survey among the members of this Association with regard to their results in resection for carcinoma of the lung, and we have sent out questionnaires and asked for a follow-up on patients who were alive and well six months or more after operation; in other words, we did not want to make the task too difficult; we felt that in that way we would eliminate those patients upon whom operation had not materially affected the course of the disease.

We have received replies on 470 patients. I would like to show the results because it adds up to a greater number of patients than any one clinic or surgeon can collect, and the results are quite germane to the present discussion. (slide.) In the 470 patients alive and well six months after operation, 123 were living and well two years or more after operation; 94 had pneumonectomies, 29 had lobectomies. There were 145 who developed recurrence or died within two years after operation, that is, between six months and twenty-four months. Then there is the question whether a two-year or thirty-month follow-up was a good follow-up period; 36 of the group of 470 patients developed recurrence or died after two years. Dividing them with respect to pnuemonectomy and lobectomy, the great majority fell by the wayside in the third year, a scattering in the fourth year, one in the fifth year, and three in the sixth year.

A group of 164 patients were alive and well less than two years after operation; of course that is an indeterminate group—we do not know which way they will go.

(Slide.) In 123 patients living and well more than two years after operation, we have classified them as to duration of survival; of 94 pneumonectomies, 20 are alive for more than five years; of 29 who had lobectomies, eight are alive more than five years following operation.

(Slide.) We were most interested in the question of node involvement. Of the 123 patients, there were no involved nodes at operation in 92, or 75 per cent; there were hilar nodes involved in 22, or 18 per cent. As you see, the duration of survival of these 22 patients indicates that at least 6 are alive over the five-year period. Of 9 patients with mediastinal and hilar node involvement (7 per cent) only 1 is alive over the five-year period, and 3 in the four- to five-year period. Then there are 145 patients who died or had recurrence from six months to two years after operation—45 per cent of whom had no node involvement at operation. Many died with metastases in distant parts of the body which is probably evidence of hematogenous spread.

We would like to go on with this survey, and we ask those men who have not sent in their questionnaires to please aid us, for we would like to accumulate a large series of cases.

DR. JOHN H. GIBBON, JR., Philadelphia.—I am very much interested in this subject. I feel as Dr. DeBakey does. When you see the slide shown by Dr. Soutter of five-year survivals, and see that there is relatively little difference between lobectomies and pneumonectomies, you might be misled to think that the authors of the paper believe that lobectomy is just as good an operation as pneumonectomy for cancer of the lung. Obviously, as Dr. DeBakey said, lobectomies can be performed only when the lesion is confined to the peripheral portions of the lung. What we are all interested in when dealing with cancer of any organ is the number of patients who survive five years in proportion to the entire number seen who have proved cancer of that organ. If, by performing a lesser operation such as lobectomy in certain selected cases where the lesion is confined to the parenchyma of the lung, one can reduce the operative mortality significantly, then perhaps one can increase the total five-year salvage rate of all the patients seen with the disease. It seems to me that is the important lesson to be learned from this series. I believe that in several of the large series of carcinoma of the lung that have been reported, 5 to 8 per cent of the entire number have survived five years. We have a small series of 276 cases of carcinoma of the lung seen in the last four years, and we can speak only of the three-year survival rate. It is in the neighborhood of 11 per cent of all the patients seen. We have performed 114 resections for cancer of the lung; all but four were pneumonectomies. Our mortality rate is 22 per cent. If we could cut that mortality rate by doing lobectomies in special types of cases, such as the authors of this paper have outlined, perhaps we could increase our total salvage rate.

DR. ALTON OCHSNER, New Orleans.—This is not the same individual making two discussions although it is the same team—I will admit that and I apologize.

Although Dr. Churchill and his associates would not want to give the impression, I fear that this discussion may do a great deal of harm, just as the discussion which is rampant at the present time in most surgical organizations as to whether one should do an anterior resection for low-lying lesions in rectal carcinomas. It is true that one can get by with them in many instances, but as Dr. Graham has emphasized, we are interested in curing patients. Everyone has emphasized this morning the desirability of doing pneumonectomy if the lesion is not limited to the lobe. Unfortunately, at the time of operation one cannot tell if the lesion is limited, and it is only after the lung is out and careful examination of the mediastinal nodes has been done that one knows whether there has been extension to these nodes. For this reason I feel that lobectomy should be limited to those cases in which pneumonectomy is contraindicated, not those in which lobectomy can be done; but if, for reasons such as a bad cardiovascular system, or if the differential study of pulmonary function would indicate that the patient could not get along with one lung, then one should do a lobectomy, and only then.

In our series of 237 cases, only 5 had lobectomies; of the 5, 3 are dead with carcinoma, 1 is living with carcinoma, and 1 apparently has no carcinoma. I would like to request that when people report statistics, that the statistics give all the cases operated upon and not only those that survive operation. Because that immediately dilutes the statistics. Why not say that these results are based upon those patients that have survived five years? That of those that survived five years, a certain percentage are still alive. Unless we include all the cases and do not consider only those that survive operation, there is dilution of statistics, which does not mean a great deal.

DR. JOHN W. STRIEDER, Brookline, Mass.—In connection with the stimulating paper of Dr. Cahan and his group at Memorial Hospital, I would like briefly to recount an experience which has seemed to us of some interest and significance. During the past year we have seen three women, each of whom had had a breast removed for cancer from two to six years prior to the time they were seen by us. Two of the patients had been followed by x-ray very faithfully; one had never had an x-ray either prior to her mastectomy or for two years subsequently. All these patients at the time they were seen by us showed pulmonary tumors which were suspicious of metastatic disease and all were explored. One proved to have an inoperable bronchiogenic carcinoma; the other two had bronchial adenomas for which restrictions could be done.

This also raises the question of what to do, in view of the known propensity of carcinoma of the breast to have multiple metastases, if shadows are present in the chest x-ray at the time the diagnosis of carcinoma of the breast is made. As Dr. Cahan has suggested, it would seem that we should have no hesitation, if there is no demonstration of multiple sites, to explore these patients at a suitable time.

MR. P. R. ALLISON, Leeds, England.—I was about three miles off the coast of America when I heard a sort of Indian war cry to the effect that Churchill was doing lobectomies for bronchial carcinoma. Anybody who has listened carefully to this most clear and precise paper presented by the Boston school today must agree that they are in fact still recommending pneumonectomy for carcinoma, and that their choice of patients for lobectomy is both reasonable and logical. I think it would be a good thing if, at the end of the discussion, they emphasized their confidence in pneumonectomy as a desirable treatment for most patients.

It is difficult to assess the importance of the two forms of treatment when they are used for different sorts of patients and different types of disease. We must also remember that the results of treatment for the last fifteen years are influenced by various cross currents. We have the antibiotics, which have had a profound influence, safe transfusions, improved anesthesia and improved technique. The effect of these lines of progress is shown in my own series, for of 101 radical pneumonectomies performed for carcinoma between 1940 and 1949, the total operative mortality was 23 per cent, but in 1948 it was only 12 per cent, and in 1949 it was 4 per cent. In the early years, trouble with the bronchial stump, producing fistula, empyema, and all its complications, turned the scale against many poor risk patients, but in the last three years the performance of 63 radical pneumonectomies for bronchial carcinoma in my unit has been associated with only one bronchial fistula. Other factors which are pertinent to this discussion are the education of the physician and the increasing use of mass radiography, which bring more early lesions to the notice of the surgeon. Of 1,050 patients with bronchial carcinoma seen between 1941 and 1948, the lung could be removed in only 7 per cent, whereas of 178 patients seen in 1949 this end could be achieved in 16 per cent.

Some further confusion in the assessment of results of lobectomy and pneumonectomy may occur from lack of definition of the terms. The description of the upper lobectomy, which Dr. Soutter has given, with dissection of the mediastinal glands, seems adequate, but pneumonectomy has not been defined. I have seen many excisions of the lung for carcinoma which, from the point of view of malignant disease, are in nowise superior to lobectomy. In these operations much good lung tissue is removed without a more radical attack on the malignant disease. We must remember that malignant cells pass through cellular tissue, lymphatic vessels, and into lymphatic glands, and that only when this is gross is it palpable. It is easy to feel in the mediastinum, find a few soft glands, and say to one's self that these are not involved, but we should remind ourselves that we need a microscope to decide this point. To do either a lobectomy or a pneumonectomy and then pick out isolated glands from the mediastinum is to forget our surgical pathology. I should like to introduce the term ''radical pneumonectomy'' as applied to malignant disease, and to emphasize that all tissues removed should be removed in continuity, as we do in other parts of the body. For many years now I have found it convenient to do such a radical pneumonectomy in continuity, by dividing the pulmonary vessels within the pericardium and removing the pericardium adjacent to the lung root with its mediastinal cellular tissue and glands attached.

In 1942, the proportion of extrapericardial and intrapericardial dissections in my clinic was six to one, but in 1948, of 22 patients operated upon, all were done by intrapericardial radical dissection in continuity, and in 1949, of 27 patients, 23 were treated in this way. At the same time as the operation has been more radical the mortality has been reduced from 23 to 4 per cent.

If circumstances such as those described by Dr. Soutter justify the performance of a lobectomy rather than a pneumonectomy, this also should be done with the most careful lymphatic dissection, but I cannot agree that the glands in the hilum of the lung can be dissected as carefully with a lobectomy as with a pneumonectomy.

DR. S. O. FREEDLANDER, *Cleveland.—My remarks shall be confined to the choice* of lobectomy for carcinoma in the poor risk patient, that is, those patients with emphysema and low respiratory reserve. It is assumed in those cases that the more lung that is left in, the better the respiratory function will be. There may be some doubt regarding this. If lobectomy is done when there is already an increased dead space due to emphysema, and that dead space is further increased by more distension of the lung, and then circulation continues in that lung, the patient will get a mixture of blood that is more poorly oxygenated than if the total lung were removed. Thus we may have more respiratory incapacity following lobectomy than following pneumonectomy in this type of patient.

DR. LEO ELOESSER, San Francisco.—It seems to me that once more the thoracic surgeons have said something of importance to general surgery. This paper of Dr. Churchill's is very important indeed; it isn't only lung cancer, but rectal cancer and breast cancer and other cancers that are involved. Perhaps by setting up rigid ideals we are doing something that is not entirely justifiable. Too often we are doing operations that are futile on the one hand and unnecessary on the other. The attempt to eradicate cancer by progressively increasing the anatomic limits of operation is not the right road to follow. We must have some regard to what happens to the man who is alive after operation. What Dr. Graham said, Shakespeare said in Coriolanus—''They that prefer a noble life before a long one . . .'' I won't give the rest of that quotation because it might spoil its pertinence here.

DR. JEROME HEAD, Chicago.—Dr. Graham has just stated that the statistics presented by Dr. Churchill and his associates are of very little significance. I do not agree with this. Any statistics are of relative value, but at the present time these are the only statistics which we have and therefore are those upon which we must work. It was very interesting to me to note that in our series of bronchiogenic carcinomas, which have just been reported by Dr. Hudson, the results are almost identical with those of Dr. Churchill and his group; namely, a 25 per cent survival rate in lobectomies and 18 per cent survival rate in pneumonectomies. The only way in which we are going to solve this question is by continuing to select cases and continuing to do pneumonectomies and lobectomies where each operation is either necessary or seems indicated. I am sure that further statistics will show better results following lobectomy, not because lobectomy is necessarily a better operation for carcinoma of the bronchus, but because of the type of case which is amenable to lobectomy. It is our practice at the present time to remove the lung where it is at all feasible. If it is necessary to open the pericardium and ligate the vessels within the pericardium, we do this. If it is necessary to remove a section of the esophagus into which the tumor has grown, we do this. After we have removed the lung, we dissect out the glands from the mediastinum. In all of these cases, in which the tumor is in a main bronchus close to the hilus, pneumonectomy is obligatory. Certainly many of the operations must be considered as palliative and certainly in a very high percentage of them all of the tumor is not removed. The cases in which lobectomy is feasible are the favorable cases. In these the hilus is not appreciably involved and one can make a relatively clean dissection. I am convinced that the lymph glands at the hilus of the lung can be removed by lobectomy as well as by pneumonectomy, and certainly the mediastinum can be dissected as well following lobectomy as following pneumonectomy. One must consider that in the individuals in the age group in which carcinoma of the bronchus most often occurs, pneumonectomy is definitely a crippling operation, whereas lobectomy is well tolerated and leaves the patient with almost normal respiratory function. For this reason I believe that lobectomy is preferable where it is feasible, even though it entails a slightly greater risk of recurrence. Personally, I would infinitely rather have a lobectomy with a 15 per cent chance of permanent recovery than a pneumonectomy with a 20 per cent chance of permanent recovery.

DR. WILLIAM M. TUTTLE, Detroit.—There can be no question but what it is an admirable thing to try to conserve lung tissue, but the question arises as to whether one should attempt too strongly to conserve lung tissue at the expense of leaving behind areas of carcinoma. It must be realized that we actually know very little about the lymphatic supply of the lung. A number of years ago Dr. Francis Phillips and I carried on some experiments on the lymphatic supply of the lung. These were never reported because the war interrupted the study. In pursuing this study a particulate matter was either injected into the lung parenchyma or placed endoscopically in a particular lung lobe. At varying intervals of time the nodes draining this area were chemically analyzed by a titration method. It was interesting to note in these studies that even when the testing material was deposited in a lower lobe of either lung it quickly reached the carinal nodes. If this study has virtue then it becomes evident that the lymphatic drainage of the lung is a relatively rapid process, and that under such circumstances pneumonectomy in the patient with cancer may offer a more curative procedure than lobectomy.

DR. CAHAN (closing).—I would like to thank Dr. Strieder for having raised ours from the rank of the forgotten paper.

DR. CHURCHILL (closing).—You will find that the published version of this paper carries no conclusions and no recommendations; it is a simple statement of facts and observations from which you can draw your own conclusions as obviously you have already done. The purpose is to present the raw data, without any attempt whatsoever to exclude cases or to divide them into those we thought we were going to cure and those for whom we thought we were going to make the remaining span of life more tolerable.

It is obvious that many variables determine the results in any individual effort to control cancer of the lung. Some of these variables can be identified today; others we may not even suspect. The extent of the removal of potentially invaded lymphatic pathways and regional lymph nodes is, of course, one variable that is of prime concern to the surgeon. It is receiving new emphasis today in all cancer surgery. We must realize, however, that we are in our infancy in knowledge concerning the lymphatic structures of the lung and hilum. No precise study has been made of the normal pathways of lymphatic flow in the different segments of the lung. Mr. Allison's remark was very apt and I agree that a total pneumonectomy may be performed in a way that makes it less effective in removing lymphatic pathways than a lobectomy, combined with a mediastinal *en bloc* resection.

Other variables must include any differential mortality rate inherent in operative procedures. If a patient succumbs to operation, he achieves no benefits from having been rid of his cancer. There is also the mutilation of function touched upon by Dr. Eloesser. The time that elapses between the inception of malignancy and its excision is, of course, a potent variable.

The prowess of the individual surgeon, assuming a reasonable degree of competence, is probably the least significant of all the variables. We are all doing about the same job with about the same results.

Certain variables that we as yet are not in a position to appraise are just coming over the horizon. These center on what is called the "degree of malignancy" which is presumably an expression of interrelationships between abnormal cell and host. This is expressed as the power of autonomous growth and ability to invade and metastasize. Personally, I am quite prepared to see new knowledge completely change the relative emphasis that we as surgeons now assign to the variables on which we set such great store.

Further, in all series of cases of cancer of the lung that have been reported, we must look with great humility upon the small number of cases that we can resect today, whatever operation we employ. An outsider looking at any grouping of results could well draw the conclusion that in arguing about the extent of the operation measured in centimeters, we have lost our way among the trees that make up the forest.

I am sorry Dr. Rienhoff is not here. We have had this argument of lobectomy vs. pneumonectomy, back and forth for years. It started at Saranac Lake when I took one of his slides showing the lymphatic system of the hilum and compared it to a swamp or a morass. I have been called a scoundrel and a rascal for the last twenty years for saying that under certain circumstances I elected to perform a lobectomy for cancer. Many visitors both from this country and abroad have discussed this matter with me and their comment very often has been, "I am glad to see that you do a lobectomy occasionally, because I do too, but I don't dare say so."

A STUDY OF PULMONARY HEMODYNAMICS DURING PULMONARY RESECTION

HARVEY J. MENDELSOHN, M.D., AND HENRY A. ZIMMERMAN, M.D., CLEVELAND, OHIO, AND (BY INVITATION) ARTHUR ADELMAN, M.D., KANSAS CITY, MO.

CARDIAC catheterization has made accessible the study of pulmonary artery and cardiac hemodynamics in human subjects with a negligible risk. Cournand, Riley, and Himmelstein[1] have studied pulmonary hemodynamics before and after pneumonectomy, in human beings, but have not observed the changes occurring during the actual operative procedure. Scarff[2] recorded pulmonary artery pressures during and after pneumonectomy in dogs. We have undertaken the study of pulmonary hemodynamics during pneumonectomy in seven cases, during lobectomy in two cases, during exploratory thoracotomy for inoperable carcinoma in one case, and during local resection of a portion of one lobe in one case. Five patients have been restudied two to six weeks after operation.

METHODS

A catheter was placed in the pulmonary artery opposite to the one to be ligated. approximately one hour before the induction of anesthesia. Basal cardiac outputs were determined by the Fick principle and initial pressures were recorded. The electrocardiogram, phase of respiration, and femoral or brachial arterial pressures were recorded simultaneously by means of a six-channel direct writing oscillograph. Subsequent observations were made at fifteen-minute intervals throughout the entire procedure, including the immediate period of ligation and after the closure of the chest. Using the Sanborn Cardioscan, the electrocardiogram was visible throughout the entire procedure.

In three cases, in which pneumonectomy was not done, the pulmonary arterial pressure measurements were obtained after temporary ligation of the pulmonary artery. In one patient a right lower lobectomy was done but the main pulmonary artery was not isolated. In the remainder of the patients, pneumonectomy was done. The pulmonary artery was first isolated and temporarily ligated, the ligature was then released. In one case the pulmonary veins were then isolated and were also temporarily ligated, and pressure readings recorded. When no appreciable change was found, this procedure was abandoned. The pulmonary artery was then ligated and divided between ligatures and the pulmonary veins were then ligated in order and divided between ligatures, and pressure readings taken following each ligation, and at the end of the procedure. Eleven days to six weeks after operation, pressures were again determined in five patients.

In one patient a catheter was temporarily introduced into the pulmonary vein that was to be ligated and thence into the left auricle (Fig. 1). No signifi-

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cant change in left atrial pressure occurred during or immediately after ligation of the pulmonary artery and veins.

RESULTS

During the induction of anesthesia, both the systolic and diastolic pressures in the pulmonary artery rose and this in some patients continued throughout the preligation period. The increase in diastolic pressure was greater than the systolic, averaging in the former 70 per cent and 36 per cent in the latter.

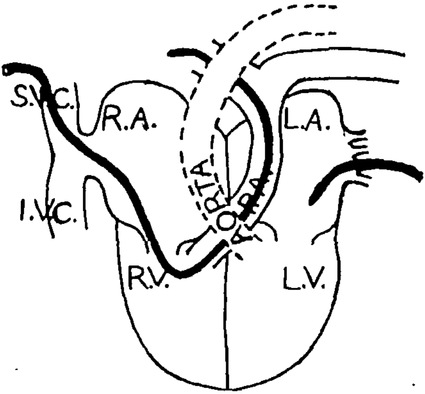


Fig. 1.—Diagram of catheters in position for taking pulmonary artery and left auricular pressures.

The rise in systolic pressure on ligation ranged from 18 to 70 per cent, the average being 40 per cent. The diastolic pressures rose from 16 to 33 per cent, except in three cases in which a decrease in diastolic pressure from 13 to 41 per cent was noted. There was a greater change in pressure, as a rule, when the right pulmonary artery was ligated as compared to the left pulmonary artery. In all except one case the pressures returned toward normal at the end of the procedure.

Table I lists the results and Fig. 2 shows the pulmonary pressures graphically in Case 8.

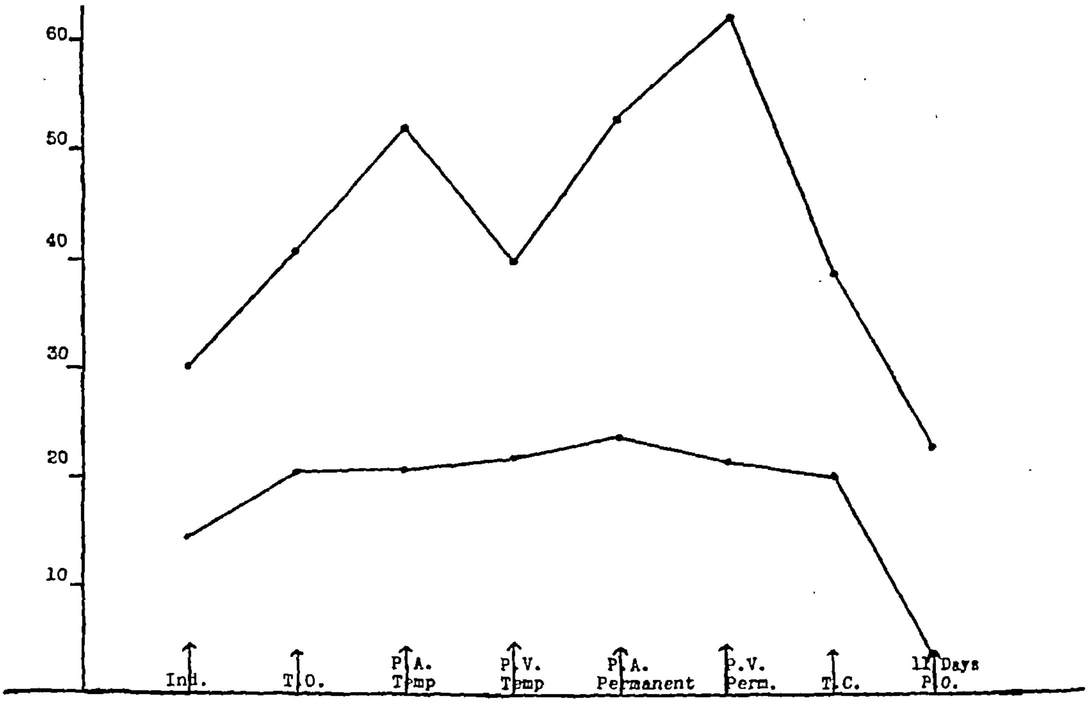
Case No. 5 (F. K.)—This patient deserves special comment. A 50-year-old white man had a small peripheral squamous-cell carcinoma of the left upper lobe which had manifested itself by severe hemoptysis. He was evaluated as a poor operative risk because of low cardiorespiratory reserve. This was evidenced by dyspnea on slight exertion, and a vital capacity of 42 per cent. Pulmonary artery pressure was twice normal but could be lowered by intravenous aminophyllin. Zimmerman and Scott[3] have shown that aminophyllin intravenously will significantly lower pulmonary hypertension due to a variety of causes. Because of this response to aminophyllin and because the electrocardiogram was normal and he had not been in congestive failure it was decided to operate upon him. A left upper lobectomy was done to preserve as much pulmonary function as possible. Fig. 3 shows the pulmonary artery pressures. Pressures rose with ligation of the lobar vessels and remained

Table I

CASE NUMBER	PATIENT		PRE-OPERATIVE	INDUCTION	THORAX OPEN	P. A. TEMPORARY	P. A. PERMANENT	CHEST CLOSED	POST-OPERATIVE
1.	M. B. 304293 54, W. M. Chr. tbc. Left pneumonectomy	P*		50/28	40/26	41/23	47/21	34/10	Died
		S′			100/59	106/60			
2.	A. S. 303427 68, W. M. Br. Ca. Part. resection R.U.L.	P*	51/14	60/32	63/34	77/34		43/27	Died
		S′	171/68	133/61	156/65	137/64		158/62	
3.	A. B. 306086 54, W. M. Br. Ca. Left pneumonectomy	P*	27/12		32/17		34/10	11/4	25/5
		S′	108/57		103/52		104/54	90/61	103/56 2 weeks
4.	W. K. 240915 54, W. M. Br. Ca. Br. Ca. Rt. pneumonectomy	P*			36/19	40/17	45/20	34/18	17/10
		S′			150/84	85/47			90/52 4 weeks
5.	F. K. 306727 50, M. W. Br. Ca. L.U. Lobectomy	P*	52/20		45/21	76/41	77/46	57/37	96/37
		S′	132/62		88/43				120/62 6 weeks
6.	H. W. 305793 49, W. F. Pulm. tbc. Left pneumonectomy	P*	23/8.4	41/26	40/21	35/24	39/22	31/18	25/11
		S′	157/90	164/120	170/118				158/91 12 days

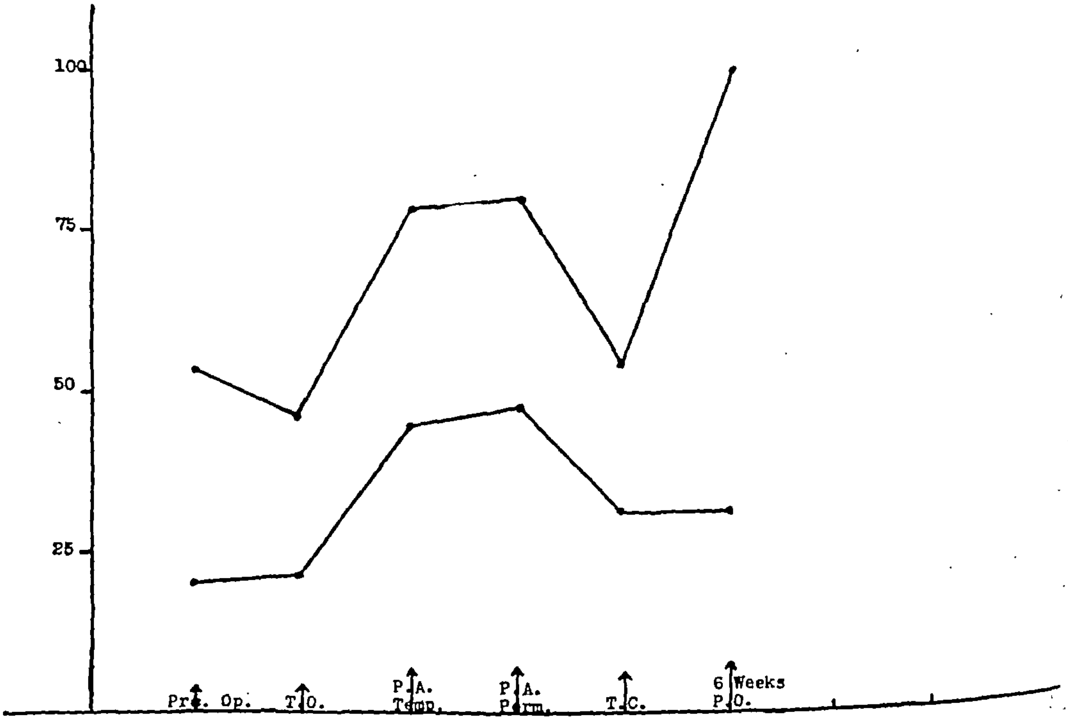
7.	J. P. 304159	P*	21/9	53/23	29/10		34/24	26/17	Unable to return, working
	30, C. M. Bronchiectasis R.L.L. and R.M. Lobectomy	S'			100/62		To lobe	80/50	
8.	J. K. 283719	P*		30/15	40/20	51/20	50/24	37/10	21/.2
	52, W. M. Br. Ca. Rt. pneumonectomy	S'		100/60	90/57	100/60	106/60	90/60	135/80
9.	F. K. 300763	P*		54/30	76/27			32/28	Died
	63, M. W. Br. Ca. Rt. Exp. Thoracotomy	S'		124/85					
10.	F. G. 309044	P*	18/5	43/24	39/25	48/26	51/27	Record unsatisfactory here	Unable to recatheterize
	55, W. M. Br. Ca. Lt. pneumonectomy	S'	103/48			90/60	96/50		
11.	H. T. 311094	P*	20/8	29/13	29/19	33/20	40/22	32/18	To be catheterized
	49, M. W. Br. Ca. Lt. pneumonectomy	S'	127/76		131/89	143/87	145/87	163/110	

P*—Pulmonary circulation, pulmonary artery pressure mm. Hg.
S'—Systemic circulation, systemic pressure mm. Hg.



Induction, Thorax open, Pulmonary artery tied temporarily, Pulmonary vein temporarily tied, Pulmonary artery tied permanently, Pulmonary vein tied permanently, Thorax closed, Post operatively.

Fig. 2 (Patient No. 8, J. K.).—Graph of changes in systolic and diastolic pulmonary artery pressures measured in millimeters of mercury.



Pre-operative, Thorax open, Pulmonary artery temporarily tied, Pulmonary artery permanently tied, Thorax closed, 6 Weeks post-operative.

Fig. 3 (Patient No. 5, F. K.).—Graph of changes in systolic and diastolic pulmonary artery pressures in millimeters of mercury showing marked postoperative *rise*.

elevated. He had a stormy postoperative course with slow re-expansion of the lower lobe. He went into congestive failure and was brought out partially by digitalis, aminophyllin, and Mercuhydrin. Six weeks after the operation the pulmonary hypertension had increased. He came back to the hospital and died eight weeks after operation in congestive heart failure due to cor pulmonale.

DISCUSSION

Hickam and Cargill[4] showed that emotion and apprehension would elevate pulmonary artery pressures in unanesthetized patients. Motley and associates[5] showed that pulmonary artery pressure rose during anoxemia induced by having patients breathe 10 per cent oxygen. This may be the explanation for the rise in pressure we observed during induction of anesthesia.

Although one would expect the ligation of one pulmonary artery to throw a heavy burden on the rest of the pulmonary vascular bed and be reflected in cardiorespiratory signs elsewhere, clinically, this is rarely the case. At pneumonectomy, when the pulmonary artery is ligated, the systemic blood pressure, pulse rate, and respiratory rate and rhythm seldom change appreciably. As demonstrated in our series recorded here and by Cournand and co-workers,[1] persistent elevation of pulmonary artery pressure following resection is not common. Our only case occurred in a patient, who had an elevated pulmonary artery pressure preoperatively.

One might theorize that this patient's preoperative pulmonary artery hypertension was equivalent to a 50 per cent or more constriction of the pulmonary artery. *Tigerstedt,[6] Fineberg and Wiggers,[7] Gibbon, Hopkinson, and Churchill,[8]* and others have demonstrated in acute animal experiments that when the pulmonary artery is constricted more than 55 per cent, circulatory failure begins to occur. Thus in this patient further diminution of the pulmonary vascular bed by left upper lobectomy could have been a major factor in precipitating congestive cardiac failure in a patient with cor pulmonale. The determination of pulmonary artery pressures may, therefore, be of help in evaluation of poor risk patients for pulmonary resection.

SUMMARY

1. Eleven patients have been studied by intracardiac catheterization of the pulmonary artery during pneumonectomy and other intrathoracic procedures.

2. During induction of anesthesia pulmonary artery pressures rose. The average increase in the systolic pressure was 36 per cent and in the diastolic pressure was 70 per cent. The average increase in the systolic pulmonary artery pressure at the time of ligation was 40 per cent; the diastolic pressure was increased an average of 5 per cent.

3. In seven patients who had pneumonectomy, the pressure returned to normal or near normal at the end of the procedure.

4. In one patient who had a lobectomy, the pressure remained elevated and the patient died of cor pulmonale and congestive failure.

5. Catheterization of the pulmonary artery in man may prove to be an important adjunct in evaluating poor risk patients for pulmonary resection.

Acknowledgment.—We are deeply indebted for technical assistance to Gladys Heckman, R.N., and Hanna Janowskovic, R.N.

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DISCUSSION

DR. AARON HIMMELSTEIN, New York.—My comment on this paper is based on studies in Dr. Cournand's laboratory at Bellevue Hospital. The results reported by the essayist concerned only pulmonary arterial pressures. In any study on circulation the blood pressures reflect the relationship of flow and resistance. When Dr. McMichael was in this country last spring, he told us that Sharpey-Schaefer had demonstrated a considerable increase in cardiac output during cyclopropane anesthesia. So far we have not found this information in published form.

I would like to show one slide which bears on the problem of flow and pressures in the pulmonary circulation (slide). In this slide the circles represent data in normal subjects. The flow is calculated as one-half of the normal cardiac output; that is the flow through one pulmonary artery. The open circles represent the resting state, the flow being about 1.5 to 2 liters. On mild exercise the flow in these patients increased to 3 liters; on exhausting exercise it went up to about 4 or 4.5 liters without any rise in pressure. Therefore, the normal pulmonary vascular bed is adaptable to these changes in flow without rise in pressure. The pulmonary capillary bed is unique among all the other capillary beds in that it is exposed to atmospheric pressure and does not receive any support from surrounding structures. In the same slide the triangular figures represent patients who have had a pneumonectomy. In these patients the remaining lung was shown to be normal by studies of pulmonary function. At rest the cardiac output of 3 to 4 liters goes through one lung only. It is seen that the pressures were normal. When these patients did a moderate exercise the flow through one lung was in excess of that through each lung of the normal subjects when performing an exhausting exercise. Then the pressures began to rise. We feel that this break in the curve defines the limits of distensibility of the pulmonary vascular bed.

DR. WILLIAM E. ADAMS, Chicago.—We have been interested in this problem for some time. I think Dr. Mendelsohn has given us some excellent information in regard to the pressure in the pulmonary arteries. We have attacked this by determining the pressure within the right ventricle; of course the object is the same, to determine in patients who need pulmonary resection for neoplastic, inflammatory, or congenital lesions, as to what their "resection tolerance" might be.

(Slide.) We have been able to get our equipment together only in time to do this on five patients, and the results are shown here in four. As he has told us, the results of changes in pressure have been about as he has indicated except that they are in the right ventricle. They changed relatively little, as you see, in most cases, two figures being given as an average. These are taken just before, during, and after ligation of the pulmonary artery. Only the first case was actually a pneumonectomy; the others happened to be inoperable carcinomas and the pulmonary artery was temporarily occluded, determining the pressures.

In the fifth case, a patient who had previously had a pneumonectomy for several arteriovenous fistulas, and had subsequently developed three or four other fistulas in the remaining lung, we removed only that portion of the lung where the fistulas were located. In this case there was a very marked rise of ventricular pressure in the right ventricle during the stage of induction of anesthesia, and somewhat less during the operation. The pressures were the same at the end of operation as at the beginning. Dr. Carlson and Dr. Charbon, my associates, have been working on this problem in animals. It is not yet ready for a complete report, but we can tell from the work so far that the pressure in the right ventricle will begin to become elevated after 50 per cent of the lung has been removed. When resection is carried further at a second operation, and it is removed to the extent of about 75 per cent, the pressures may go up as much as 100 per cent. This elevation is sustained. If it is carried further, leaving only one lobe, an upper lobe inflated, the pressures will go still higher.

A number of these animals have survived and have been followed for several months. The pressures have remained elevated. We cannot compare a normal dog's lung with the lung of a patient of advanced years where there is emphysema and degenerative changes. I would consider that a dog with 50 per cent of the normal lung removed might be in about the stage of a patient at the beginning, when we are faced with his therapy. From that standpoint, if we can determine a means of measuring his pulmonary resection tolerance by a test such as this, it will help us, especially in those cases where we have a choice of operation.

DR. JEROME HEAD, Chicago.—These studies have been very interesting in that they have helped to explain certain things which I have observed at operation. Not infrequently at the present time in resecting the lung one finds it necessary to open the pericardium and ligate the pulmonary vessels close to the chambers of the heart. In a number of the cases in which I have done this, I have noted that the heart herniates through the pericardium, often to such an extent that one fears for its integrity. This means that at this point in the operation the heart is attempting to dilate and that it is being restricted by the pericardium. It means, in other words, that often during a pneumonectomy there is a definite cardiac tamponade. The observation suggests that the pericardium has a very definite function in preventing overdilatation of the heart and that under conditions of extreme strain it confines the heart within reasonable limits and prevents cardiac damage. It suggests that one must consider the pericardium as an elastic capsule which stretches quite rapidly but quite gradually, permitting sudden strains which are thrown upon the heart to be accommodated gradually rather than suddenly.

DR. MENDELSOHN (closing).—I wish to thank Dr. Himmelstein, Dr. Adams, and Dr. Head for their comments. We are pleased that Dr. Adams' findings confirm ours. However, we do not recommend leaving a catheter tip in the right ventricle for any length of time. This is dangerous and may produce ectopic beats or rhythms.

CONSERVATIVE MANAGEMENT OF EMPYEMA FOLLOWING TOTAL PNEUMONECTOMY

EDWARD M. KENT, M.D.
PITTSBURGH, PA.

THORACIC empyema as a complication following total pneumonectomy has been a very disturbing event although one of decreasing frequency in recent years. In the majority of instances such a complication has been associated with a bronchial fistula, although about one-third of the cases to be reported herein did not have demonstrable leaks in the bronchial stump. Heretofore, it has been widespread practice to combat such an empyema by the application of established principles of surgical management. Since there is no longer a lung to be expanded, thus obliterating the infected pleural cavity, a radical thoracoplasty has been employed to achieve this end. It has been our experience that a conservative regime employing local instillation of antibiotics has made thoracoplasty unnecessary in the majority of patients treated. It is apparent that these observations are at variance with our concepts of the established rules in the surgical management of thoracic empyema; nevertheless, the results of this therapeutic regime have been very favorable in a small series of 19 patients.

There has been a certain amount of discussion concerning the role of a bronchopleural fistula as the cause of infection of the pleural space. Some believe that a postpneumonectomy infection of the pleural space which is associated with a leak in the stump of the bronchus can be considered to have occurred as a result of contamination from the tracheobronchial tree through the opening in the bronchial stump. Others believe that the bronchial fistula is the result of infection, either at the site of the closure of the bronchus or in the empty pleural space. It is my opinion that either sequence of events may take place and that, as a rule, a bronchial fistula which occurs within the first ten days after operation is a true failure of healing in the bronchial stump and that the associated empyema is of secondary origin. On the other hand, in those instances of a later leak in the bronchus, usually from three to five weeks after pneumonectomy, the cause is most commonly infection in the pleural cavity with an empyema which escapes through the recently healed bronchus. In these days of antibiotics, such an empyema is often essentially silent. Since the patient is almost always at home by this time, it has been unsuspected in most instances until the bronchus opens. Yet, the evidences of established infection are usually present at the onset of the bronchial leak, with purulent fluid present upon thoracentesis and in the expectorated material.

For purposes of analysis, the patients comprising the series to be presented herein have been divided into two groups. The first group includes those which presented an open bronchus and the second group is composed of

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those patients who developed thoracic empyema following pneumonectomy without demonstrable bronchial fistulas. The period of observation extends over the past sixty-four months.

GROUP I. EMPYEMA ASSOCIATED WITH BRONCHIAL FISTULA

Thirteen patients have been treated for thoracic empyemas accompanied by a leak of the stump of the bronchus. Success has hinged upon the fact that in every instance the bronchial fistula healed after institution of surgical treatment by means of a rib resection and open drainage. Closure of the bronchus has occurred within ten days after drainage had been established. This observation alone has been most satisfying and I cannot be certain of the *causes of these observations. For repair of the bronchus at the time of pneumonectomy* I have employed standardized techniques for the most part; nevertheless, a review of the method is in order.

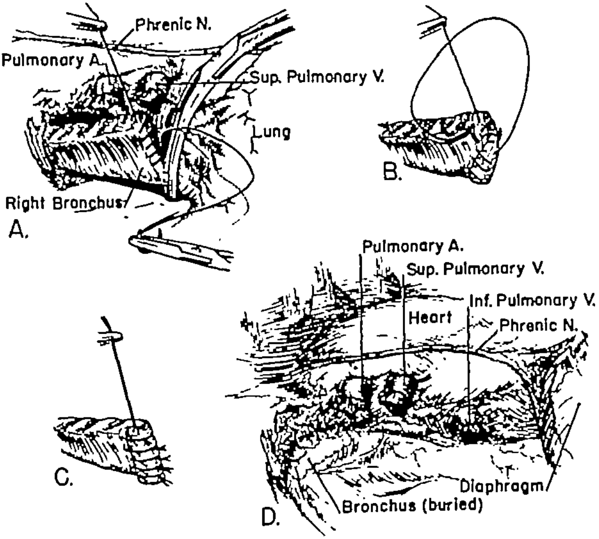

Fig. 1.—*A*, Closure of the bronchus as it is severed. No clamps are applied to proximal stump of bronchus.

B, A second row of continuous sutures is employed to fold the stump of the bronchus upon itself.

C, A row of interrupted silk sutures is placed in bronchial stump.

D, Bronchus is buried in the mediastinum.

Clamps on the proximal stump of the bronchus are avoided (Fig. 1, *A*) and a continuous suture of chromic No. 0 swaged on a curved intestinal needle is placed along the open end of the bronchial stump, step by step, as the bronchus is severed. This achieves approximation of the walls of the bronchus at the end in precise fashion by means of shallow bites with the needle. When this row has been completed, the same suture is carried back across the end of the bronchus using deeper bites and folding the end of the bronchial stump over upon itself (Fig. 1, *B*). Last, a row of interrupted fine silk sutures is placed, and these are tied over the end of the bronchus (Fig. 1, *C*). The closed bronchial stump is then buried in the mediastinum by approximating the mediastinal pleura and whatever connective tissue is available and suitable for the purpose (Fig. 1, *D*).

It is not always possible to fold the end of the bronchus over upon itself. In some instances the stump is too short to permit folding, especially when pneumonectomy has been performed for carcinoma, and particularly when a right pneumonectomy has been done because of the short stump usually available on that side. Furthermore, the older the patient the more rigid the wall of the bronchus is likely to be and accordingly, less easily folded upon itself. I have no records to indicate which of the patients in this group had the benefits of folding over of the bronchial stump upon closure and which, if any, did not. When it was not possible to double the end of the bronchus upon itself, the closure was as described above in all other respects.

The steps in the plan of treatment consist of the following:

1. Thoracostomy for surgical drainage.
2. Instillation of antibiotics through the drainage tube after the bronchial fistula has closed.
3. Removal of the tube and continued instillation of antibiotics into the pleural cavity through the chest wall.

In the presence of a bronchial fistula, cultures of the empyema fluid customarily reveal mixed infections to be present. Once the opening in the bronchus has closed, antibiotics are instilled into the pleural cavity through the drainage tube. An empirical dosage including 200,000 units of penicillin and one-half gram of streptomycin has been employed in a single daily administration. This is continued until the drainage has become reduced in volume and less purulent in character. Cultures are taken periodically and when the preceding changes in amount and character of the drainage can be coupled with bacteriologic cultures yielding a change of flora, the drainage tube is removed. Thereafter, the same dosage of antibiotics is instilled into the pleural space through the chest wall, usually in the second interspace anteriorly. The change in flora noted previously commonly shows one of the staphylococci or other organisms which may be considered as contaminants. The time period for this step has averaged ten days.

In some instances, loculations and fibrin masses will be present in the pleural cavity when the bronchus has healed. Under these circumstances, Dakin's solution has been employed as an irrigant twice daily until the empyema space has been cleansed of all such media for bacterial growth. Fluoroscopic examination and thoracoscopic inspection through the drainage tract will yield the necessary information in this regard. Antibiotic therapy is delayed until this has been accomplished in those instances in which loculation and fibrin deposits have persisted.

Once the tube has been removed, the use of antibiotics by injection into the pleural cavity is continued as a single daily dose for one week. The patient is then observed a few additional days for any evidence of fever and by fluoroscopic examination for indications of an increase in the amount of fluid in the pleural cavity. In no case has either finding been observed.

In this group of 13 patients, the fistula occurred within ten days in 6, and after a longer period in 7 (Table I). As has been stated previously, the fistula closed in each instance after surgical drainage had been established. One patient experienced a recurrence of the empyema three and one-half months after release from the hospital but without reopening of the bronchus. He was treated successfully a second time by the same method and has remained well for twenty-two months. A second patient had a recurrence of empyema without fistula and has refused to undergo a second course of treatment or a thoracoplasty. He is still wearing a drainage tube. A third patient was treated as an ambulatory out-patient, at my suggestion, by his personal physician. A recurrence was experienced shortly after the tube was removed, which was successfully treated at a later date. The details of this case are to be presented more completely because of the unusual observation that the empyema first occurred nineteen months after pneumonectomy. A fourth patient was treated by this method but the character, volume, and cultural findings were not influenced by therapy and a thoracoplasty was performed. At the time, neither bacitracin nor aureomycin was available and in the light of recent experiences, I believe he might have been treated successfully by these newer antibiotics. This case will be presented in some detail also because the empyema occurred eight months after pneumonectomy had been performed.

Therefore, in this group of 13 patients, 11 were cured of empyema by conservative means while 1 required a thoracoplasty and 1 is still carrying a thoracostomy tube after a recurrence of empyema following therapy. Two

TABLE I. RESULTS OF TREATMENT IN THIRTEEN PATIENTS WHO DEVELOPED BRONCHIAL FISTULAS AND EMPYEMAS AFTER TOTAL PNEUMONECTOMY (A MIXED INFECTION WAS PRESENT IN ALL CASES)

PATIENT	AGE (YEARS)	PATHOLOGY	ONSET OF EMPYEMA AFTER PNEUMONECTOMY	RESULT	COMMENT
1. W. C.	28	Lung abscess	8 months	Failure	Thoracoplasty
2. O. R.	50	Carcinoma	19 months	Cure	1 recurrence, cured
3. W. B.	64	Carcinoma	5 weeks	Recurrence	Refuses further treatment
4. A. J.	60	Carcinoma	10 days	Cure	Successful treatment after one recurrence
5. B. L.	52	Carcinoma	8 days	Cure	
6. F. R.	46	Carcinoma	7 days	Cure	
7. E. D.	49	Carcinoma	10 days	Cure	
8. J. R.	36	Bronchiectasis	9 days	Cure	
9. L. S.	56	Carcinoma	8 days	Cure	
10. J. B.	48	Multiple abscesses	4 weeks	Cure	
11. R. D.	46	Carcinoma	5½ weeks	Cure	
12. J. K.	26	Bronchiectasis	4½ weeks	Cure	
13. B. F.	39	Lung abscess	6½ weeks	Cure	

additional patients in this group experienced recurrence of the empyema but both were cured by a second course of therapy.

Bacteriologic control of progress of treatment can be provided with ease in most instances during the last phase of therapy. When the needle is inserted into the pleural cavity for the purpose of injecting the antibiotics, a specimen of the pleural fluid may be obtained first and culture studies can be made. This also permits observation of changes in the gross character of the residual effusion. Usually, the fluid soon becomes thin and clear but retains the color of the antibiotics. However, in three patients, aureomycin has been introduced into the cavity and the fluid has become grossly bloody in each instance.

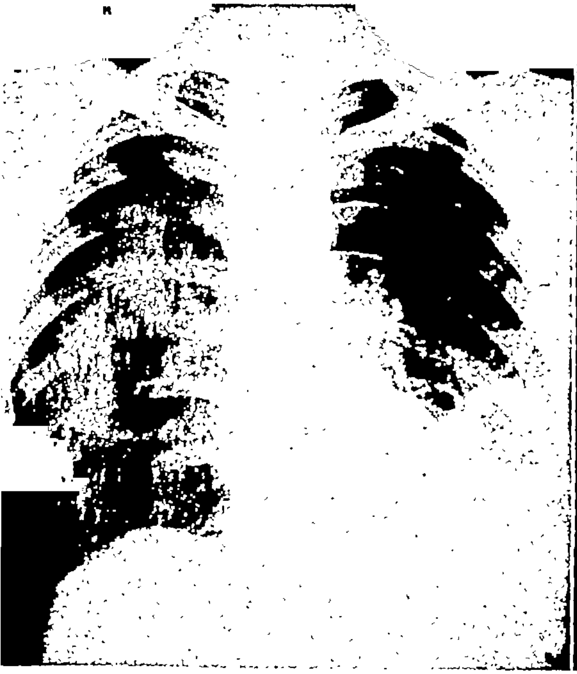

Fig. 2.

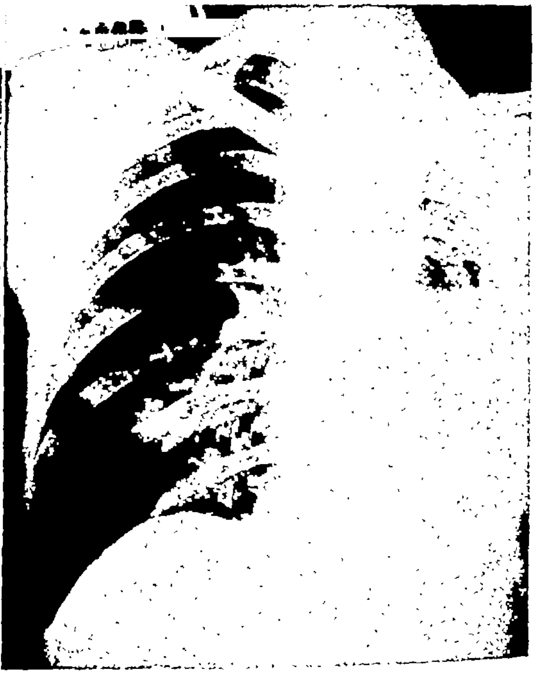

Fig. 3.

Fig. 2.—Roentgenogram of chest showing large, thick-walled cavity in lower left lung.

Fig. 3.—Roentgenogram of chest showing fluid level in left thoracic cavity and infection of remaining right lung.

CASE REPORTS

Case No. 1.—W. C., male, aged 28 years, was admitted to the hospital with symptoms of pulmonary suppuration which had persisted for three months. The cause of onset was unknown. Marked pulmonary osteoarthropathy was manifest in many joints. A chest film revealed a large, thick-walled cavity, apparently limited to the left lower lobe. After thorough study, a diagnosis of pulmonary abscess was made and an aggressive course of therapy was pursued. Despite adequate treatment, the abscess cavity persisted (Fig. 2) and the symptoms continued with little change. Accordingly, resection of the left lower lobe was decided upon and operation was performed April 7, 1948. At the time of operation, it was established that the abscess cavity had extended across the interlobar fissure into the lingula of the upper lobe and that a large excavation had occurred in this segment. A total pneumonectomy was performed and an uneventful convalescence was marked by very rapid disappearance of the signs and symptoms of pulmonary osteoarthropathy. Eight months later, the patient was readmitted to the hospital. He then presented a history of very marked recurrence of the symptoms of pulmonary suppuration with the onset having taken place ten days previously. Clinical evaluation soon demonstrated the presence of empyema (mixed infection) in the left pleural space, an associated fistula in the bronchial stump, and spill-over infection of the right lung (Fig. 3). Drainage of the left empyema was performed at once and bronchoscopic aspiration for the infection in the right lung soon followed. Systemic antibiotic therapy had been instituted upon admission to the hospital. The infection in the right lung cleared rapidly and the fistula in the bronchial stump closed within seven days. Attempts were made to employ the conservative regime of antibiotic therapy by instillation into the pleural cavity, using both penicillin and streptomycin. The volume, character, and culture characteristics were not affected by treatment and a thoracoplasty was performed. If aureomycin or bacitracin, or both, had been available for use, it might well have been possible to avoid thoracoplasty.

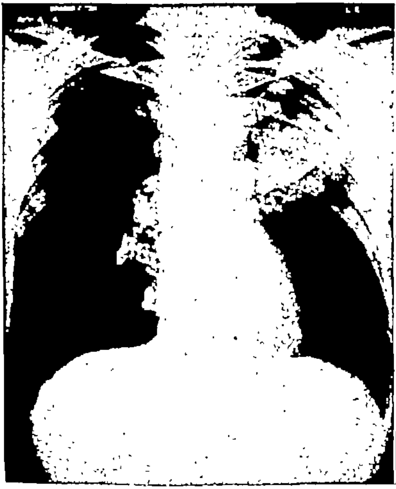

Fig. 4.

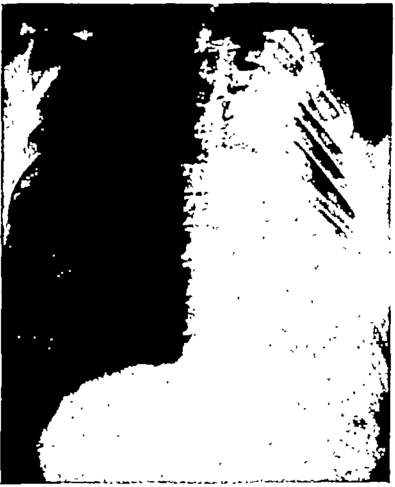

Fig. 5.

Fig. 4.—Roentgenogram of chest showing mass in left upper lobe. This was proved to be due to squamous-cell carcinoma.

Fig. 5.—Roentgenogram of chest showing empty left thoracic cavity after evacuation of of contents through the stump of the bronchus twenty-two months following total pneumonectomy.

Case No. 2.—O. R., male, aged 50 years, was admitted to the hospital on April 4, 1947 with a history of cough, expectoration, and hemoptysis of three months' duration. Clinical study established a diagnosis of squamous-cell carcinoma, left upper lobe bronchus (Fig. 4). A left total pneumonectomy was performed on April 11, 1947, and an uneventful convalescence followed. Nineteen months later, there was sudden onset of fever of unexplained origin which was treated by penicillin, aureomycin, and streptomycin in large doses. The fever persisted until early February, 1949, at which time the patient coughed up a large quantity of bloody pus. Thereafter, cough persisted but the temperature was normal. He was readmitted to the hospital on March 3, 1949, and clinical study revealed an empyema on the left side (Fig. 5) with a fistula in the bronchial stump. Rib resection was performed and open drainage was established. The bronchial fistula healed promptly and the patient was released from the hospital after arrangements had been made for treatment of the empyema cavity by instillation of penicillin and streptomycin under the guidance of his own physician in his home city. However, when the tube was removed, a recurrence of fever was noticed within twenty-four hours and the tube was reinserted by his physician within seventy-two hours. The patient elected to carry the drainage tube for eleven months, after which he returned to the hospital under my care for a thoracoplasty. After discussing the problem, the patient elected to accept one more attempt to correct the left empyema by conservative means. Since both penicillin and streptomycin had been introduced into the thoracostomy tube daily during the entire period, it was assumed that the invading organisms had developed resistance to these antibiotics. Consequently, it was decided to employ bacitracin in doses of 25,000 units daily as long as the drainage tube was in place. After the tube was removed, this drug was replaced by aureomycin (soluble, for parenteral use) in doses of 100 mg. daily into the pleural cavity. A good result was achieved on this attempt and the patient has been well for four and one-half months. Since the first empyema was so late, it may be said that it is still too early to be certain of the end result.

In addition to this group of 13 patients who have developed empyemas and bronchial fistulas after total pneumonectomy, three more instances of leakage of the bronchial stump have been experienced but none has been treated by this method for differing reasons. One patient died of suffocation on the day the bronchus failed (fifteen days after pneumonectomy for carcinoma). A second patient never developed infection of the pleural space, and a plastic closure of the bronchial fistula was performed. The third patient still has a bronchial fistula which occurred one month after right pneumonectomy for carcinoma in September, 1949; there is evidence of advancing metastases and I suspect that a recurrence in the stump may have caused the fistula and probably explains the failure of the bronchus to heal.

GROUP II. EMPYEMA WITHOUT BRONCHIAL FISTULA

A group of 6 patients have been observed, all of whom have developed empyema following total pneumonectomy but without evidence of a leak in the bronchus. With the exception of one patient, all were proved to have a pure infection after culture studies (Table II). In each instance, the empyema was not manifested for at least a month after operation. The same program of treat-

TABLE II. RESULTS OF TREATMENT IN SIX PATIENTS WHO DEVELOPED EMPYEMAS WITHOUT BRONCHIAL FISTULAS AFTER TOTAL PNEUMONECTOMY (PURE INFECTION IN FIVE CASES, MIXED INFECTION IN ONE CASE)

PATIENT	AGE (YEARS)	PATHOLOGY	ONSET OF EMPYEMA AFTER PNEUMONECTOMY (DAYS)	RESULT	COMMENT
14. A. C.	44	Carcinoma	105	Failure	2 *recurrences* (hemolytic *Staph. aureus*)
15. W. H.	61	Carcinoma	35	Cure	Empyema necessitatis. (mixed infection)
16. M. Y.	46	Bronchiectasis	16	Cure	(Hemolytic *Staph. aureus*)
17. B. K.	60	Carcinoma	38	Cure	(Pneumococcus) Empyema necessitans
18. R. L.	29	Lung abscess	26	Cure	(*Hemolytic Staph. aucrus*)
19. F. R.	48	Carcinoma	19	Cure	(*Stap. albus*)

ment has been pursued except that it has been unnecessary to await closure of a bronchial fistula after drainage of the empyema. All have responded well to therapy, except one patient who has had two recurrences as reported below.

CASE REPORT

CASE No. 14.—A. C., female, aged 44 years, was admitted to the hospital June 8, 1947, with a history of cough, expectoration, hemoptysis, fever, and weight loss. Bronchoscopy and biopsy yielded a diagnosis of carcinoma of the right main bronchus. A right total pneumonectomy was performed which was followed by an uneventful convalescence. Sixteen weeks later she was readmitted to the hospital with a history of onset of high temperature five days previously. A diagnosis of right empyema was established and drainage by rib resection was employed. A program of local instillation of antibiotics (penicillin and streptomycin) was pursued with a good initial result. The cultures had shown pure growth of a hemolytic *Staphylococcus aureus.* Three months after her return home, a similar episode occurred and spontaneous evacuation of pus took place through the site of the rib resection which had been performed previously. She was readmitted to the hospital and a second regime of local antibiotic therapy was carried out. The cultures at the time of recurrence again revealed pure growth of a hemolytic *Staph. aureus.* A good primary result was achieved once more and the patient was released from the hospital only to experience a second recurrence three months later. Once more the cultures revealed only a hemolytic *Staph. aureus.* After drainage had been re-established, a thoracoplasty was performed with subsequent control of the empyema.

DISCUSSION

The treatment of empyema thoracis by the use of antibiotics and without surgical drainage has met varying responses. Blades, Hamilton, and Dugan,[1] Roberts, Tubbs, and Bates,[2] and Poppe[3] have reported unfavorably on the matter while Burnett, Rosemond, Hall, and Caswell,[4] Lockwood, White, and Murphy,[5] and Hirshfeld, Boggs, Abbott, and Pilling[6] have recorded promising results. It has been my experience that such a plan of conservative management is effective if the empyema is not too extensive, if treatment is begun early in the course of the disease, if there is no loculation, if the pus is not thick, and if adequate, aggressive therapy is applied throughout the treatment period. In brief, the factors must be such that prompt and complete re-expansion of the lung is achieved while aspiration therapy is employed. If obliteration of the pleural space cannot be effected readily, treatment is likely to fail or the end results may be unsatisfactory.

After total pneumonectomy has been performed, there is no lung to obliterate the pleural cavity in combating infection of that space. Therefore, the essential mechanism of healing in empyema thoracis cannot be brought about, and in order that the space may be obliterated, a thoracoplasty has been deemed mandatory. The studies reported indicate that it is not always necessary to obliterate the pleural space in order to cure an empyema which follows total pneumonectomy, provided there is no leak in the bronchial stump. I cannot conceive of this form of treatment being either safe or successful if a bronchial fistula is present.

The bacteriologic procedures which have been employed in this study have been limited in scope and application. For example, no tests have been carried out to ascertain the degree of sensitivity of organisms to antibiotics.

Certainly more adequate use of the techniques practiced in bacteriology will extend the effectiveness of such therapeutic measures as these.

SUMMARY

1. The conservative treatment of empyema following total pneumonectomy has been outlined.
2. Nineteen patients have been treated by this method with sixteen successful end results. There has been no mortality.
3. Three patients have been followed for five months or less, the remaining thirteen patients have been observed for nine or more months.
4. Bronchial fistulas associated with empyemas have been found to heal after surgical drainage of the infected pleural space.
5. More adequate use of the techniques of bacteriology should improve the results of this form of treatment.

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DISCUSSION

DR. DAVID WATERMAN, Knoxville, Tenn.—I am impressed in two ways by this excellent paper of Dr. Kent's. In the first place I think it illustrates again the fact that our concepts of clinical therapy are still in a fluid state with regard to antibiotic therapy. In the second place, I think it demonstrates one of the primary obligations of the surgeon—to avoid surgery if that is possible. Generally speaking, the principle of drainage, of course, is still a valid one. Occasionally, in an early empyema occurring after pneumonectomy, even open drainage may be circumvented, despite the fact that it has been unequivocally stated that obliteration of the pleural space is essential if the empyema is to be healed. I would like to show slides of a case illustrative of such an instance, done a number of years before we realized the usual limitations of antibiotic therapy.

(Slide.) This is a 43-year-old man who came to us six years ago with multiple lung abscesses involving all three lobes on the right. He was desperately ill, and had to go through a long period of hospitalization with repeated bronchoscopies before he could be safely brought to surgery. (Slide.) This is the injection of the pneumonectomy specimen showing almost complete destruction of the normal architecture of the lung. As I recall there were 16 cavities present. (Slide.) A few days postoperatively, at the time the roentgenogram shown here was taken, he developed staphylococcus empyema.

Being brash in those days because of the early reports on the use of penicillin in empyema, we attempted to treat the patient conservatively without drainage, and injected penicillin daily into the pleural space in the same way we may very occasionally successfully do it in early postpneumonia empyema.

After some ten days of treatment, several sterile cultures were returned, and the patient was sent home. About two weeks later he had a recurrence of empyema and came back into the hospital. Again he was treated conservatively, and the empyema was successfully sterilized in spite of the fact that a large free pleural space continued for some time thereafter. (Slide.) Here is the final result more than five years after therapy. The patient has been well and working during this entire period.

The essential requirement for such results, of course, is an early empyema caused by a penicillin-sensitive organism. Once loculation has occurred, drainage is obligatory.

As to the bronchial closure Dr. Kent has described, I do not think the type of suture is as important as the avoidance of bronchial traumatization, and the adequate covering of the stump. For several years we have used with marked success a free pleural graft tied over the cut edge of the bronchus with the bronchial closure sutures. This interposes an effective barrier between the bronchus and the surrounding vascular structures. Should a stump abscess occur, the danger of erosion into a vessel is lessened, we believe.

DR. L. R. DAVIDSON, New York.—In that Dr. Kent has presented the problem of bronchopleural fistula and its complications, it gives me an opportunity to tell of a conservative method of therapy which has been used at Seaview Hospital at the instance of Dr. Warner. Taken from the pathologic sense we have applied it clinically. It is well known that lye or sodium hydroxide is markedly sclerotic. Therefore, with that in mind, Dr. Warner suggested the application of a bead of sodium hydroxide to the bronchial stump. In these cases of bronchopleural fistulas following excisional surgery, the results to date, so far as I could gather shortly before I left New York, were as follows:

The total number of cases treated, 24; closures to date, 15; patients in good condition, sputum negative and fistula closing, 2; closing, but contralateral lesion with positive sputum, 3; patient in good condition, bronchus closing clinically, 1; 4 deaths.

If you add those figures, although I mentioned 24 cases, the figure will be 25, the reason for the discrepancy being that one case after closure died of a spontaneous pneumothorax on the opposite side. We have had some cases where, in the presence of a contralateral pneumothorax, we have gone ahead and performed pneumonectomy.

The method of treatment is this: One takes a metal stylet, heats it, puts it into a *can of lye and forms a bead. Through the bronchoscope the bead is applied to the stump,* and after 30 to 45 seconds a sponge upon a bronchoscopic holder, saturated and then dried, with 6 per cent acetic acid, is applied to the area originally touched by the sodium hydroxide; that is to neutralize it. Applications are made usually two to three weeks apart and, on the average, two to three applications are necessary.

We mention this procedure with no particular claim for oringinality or for success, but merely as a method of attempting to close these bronchopleural fistulas, which do occur regardless of the technique of closure for pulmonary tuberculosis.

DR. JOSEPH WEINBERG, Van Nuys, Calif.—Dr. Kent has reported excellent results in the treatment of chronic empyema by a carefully planned method of antibiotic therapy. However, it should be kept in mind that the period of follow-up observation is short, and it is too early to predict that the empyemas so treated will remain healed. It has been a not uncommon experience to have empyemas supposedly healed by antibiotic therapy, particularly penicillin therapy, recur after a dormant period of months or years. Especially has this been the case in those patients in whom the pleural space has not been obliterated. Whether this will be the case with Dr. Kent's more studied plan of treatment with antibiotics other than penicillin remains to be seen.

A most welcome phase of the treatment described is the closure of bronchial fistula which may coexist with the empyema. For those cases in which the bronchial fistula fails to close with nonsurgical treatment, I wish to present a simple surgical method of effecting closure. The thickened parietal pleura which surrounds the fistulous opening is removed by decortication— preferably removing the entire parietal pleural membrane to favor healing of the coexisting empyema. This leaves a cuff of the bronchus projecting into the pleural space. One can then close the bronchus by suture according to his preferred method. We have successfully closed two fistulas in this manner. One followed pneumonectomy for carcinoma, with repair ten months after pneumonectomy. The other followed pneumonectomy for abscess associated with extensive bronchiectasis, with repair approximately two years after resection. The fistulas remain closed ten months and one month, respectively, after repair.

THE UTILIZATION OF STREPTOKINASE-STREPTODORNASE

IN A PATIENT WITH HEMOPNEUMOTHORAX AND A PATIENT WITH POSTPNEUMONECTOMY SANGUINEOUS COAGULUM

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NEW YORK, N. Y.

THE rapid lysis of blood clots and related coagulum of exudates takes place, as shown by Tillett and Sherry,[1] when concentrated and partially purified preparations derived from broth cultures of hemolytic streptococci are instilled into them. These preparations are unique in their action in that they show rapid lysis of fibrin clots, alter fibrinogen so that it no longer forms fibrin, and cause the insoluble fibrouslike nucleoprotein found in purulent collections to dissolve.

The fibrinolytic activity of hemolytic streptococci was discovered by Tillett and Garner[2] but only recently has this property been extensively purified and concentrated by Christensen.[3] The filtrates containing the active principles are recovered from broth cultures in large amounts, free of bacteria. More recently Sherry, Tillett, and Christensen[4] showed a significant constituent present in pus consisted of desoxyribonucleoprotein, forming 30 to 70 per cent of purulent sediment. Tillett, Sherry, and Christensen[5] demonstrated a second enzyme, streptodornase, that changed the thick viscid nucleoprotein to a thin solution.

The streptococcal fibrinolysin product has been termed "Streptokinase" and the nucleoprotein lysing factor "Streptodornase."

Although the enzymatic activity is chiefly present in human Group A hemolytic streptococci, the products under discussion are derived from the Lancefield Group C, H46A strain since it is a nonpathogen for man and would, therefore, be least likely to obscure the clinical picture by any serious toxic side-reactions.

Streptokinase acts very much like a catalyst but it is depleted as the dissolution of the parent substance takes place. Consequently its action in patients is self-terminating. It has been shown that a precursor present in bloody collections and exudates termed plasminogen or activatable fibrin-lysing system is needed to effect fibrin lysis. This is illustrated in experimental studies by the failure of a clot to lyse when highly purified fibrinogen and thrombin are mixed with SK (streptokinase). However, with the addition of plasma Fraction III, which contains the plasminogen, lysis ocurs quickly. No activatable substance is required for the lysis of the nucleoprotein per se since SD (streptodornase) is an active enzyme.

From the Chest Surgical Service, Columbia University College of Physicians & Surgeons, Bellevue Hospital, and the Third Medical and Surgical Divisions, New York University College of Medicine, Bellevue Hospital.

This study was supported under a contract with the Department of the Army, Office of the Surgeon General United States Army.

Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

The enzymes used in the early studies were produced in the laboratory of Dr. Christensen but more recently sufficient amounts are being manufactured commercially* to carry on large scale clinical studies. The details of the purification and the original investigative results with the enzymes appear in earlier reports by Tillett and Sherry[1, 5, 6, 7] and Christensen.[8] In a forthcoming report by Tillett, Sherry, and their associates† a comprehensive analysis of the dosage, laboratory findings, and a review of clinical data relative to hemothorax will be discussed.

The enzymes as now prepared in lyophilized form appear mixed together *with varying amounts of either increment but usually with predominant portions* of SK. Although probably not required in cases of hemothorax the presence of SD is not contraindicated nor does it detract from the action of SK. In this report we are essentially interested in the clinical application of SK.

On the Chest Surgical Service, and others, at Bellevue Hospital and at neighboring institutions where the material has been allotted by and used under the direction of Dr. W. S. Tillett and those associated in the work, SK has been used in a number of patients. The results for the most part have been good and in several instances dramatic. Two cases of this group are described here in which it was used.

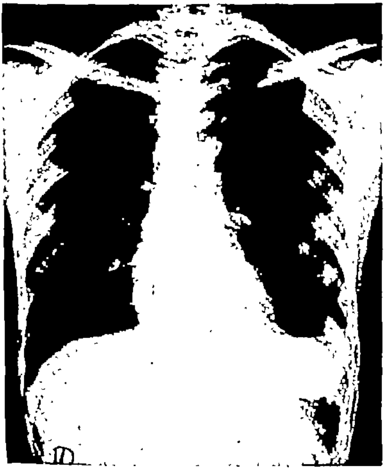

Fig. 1.

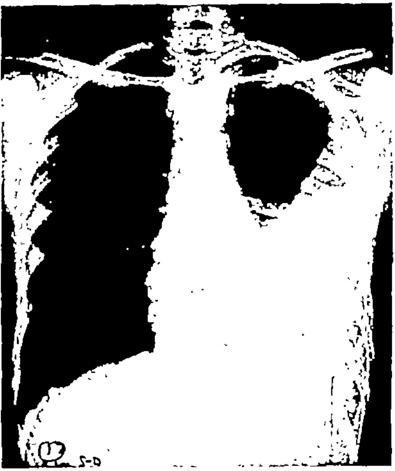

Fig. 2.

Fig. 1 (Patient M.L.).—X-ray appearance on the day of admission showing about 40 per cent pneumothorax and a small amount of fluid at the left costophrenic angle. Subsequent to this film a large accumulation of blood appeared in the space.

Fig. 2 (Patient M.L.).—Roentgenogram of chest taken on the seventeenth hospital day just before the use of enzyme therapy, showing an extensive density from which only small quantities of bloody fluid could be aspirated on numerous attempts.

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*Lederle Laboratories, Inc., Pearl River, N. Y.

†In preparation, Tillett and co-workers.

CASE REPORTS

PATIENT M. L.—This 21-year-old colored man,* without any previous pulmonary complaints, was admitted on Sept. 8, 1949, to St. Vincent's Hospital two hours after the acute onset of pain in the left chest. There were no other symptoms. The admission x-ray and fluoroscopic examination showed a 40 per cent pneumothorax in the left hemithorax and a small collection of fluid at the costophrenic angle (Fig. 1).

On Sept. 9, 1949, the roentgenogram showed about an 80 per cent hydropneumothorax; 1,200 c.c. of bloody fluid and air were aspirated from the hemothorax and a similar yield was obtained the following day. At this time his temperature ranged between 101° to 102° F. but all cultures of fluid withdrawn were negative.

Thereafter only small quantities of serosanguineous fluid could be aspirated. By the seventeenth hospital day, the roentgenogram still revealed an extensive coagulum in the left chest (Fig. 2).

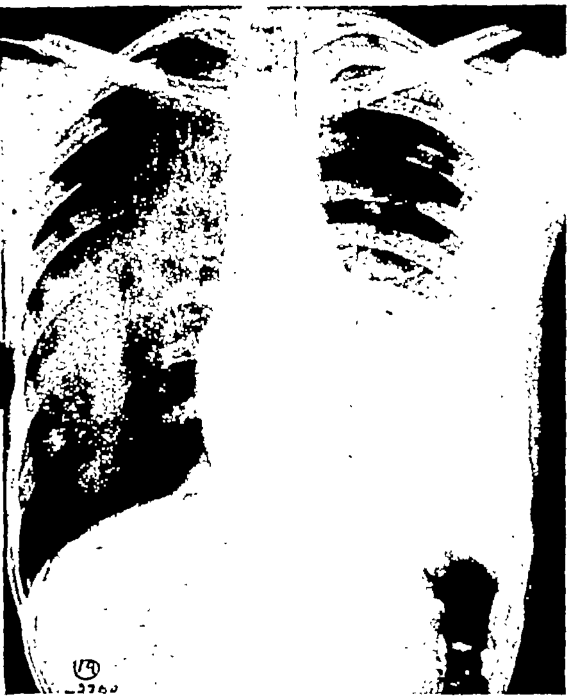

Fig. 3.

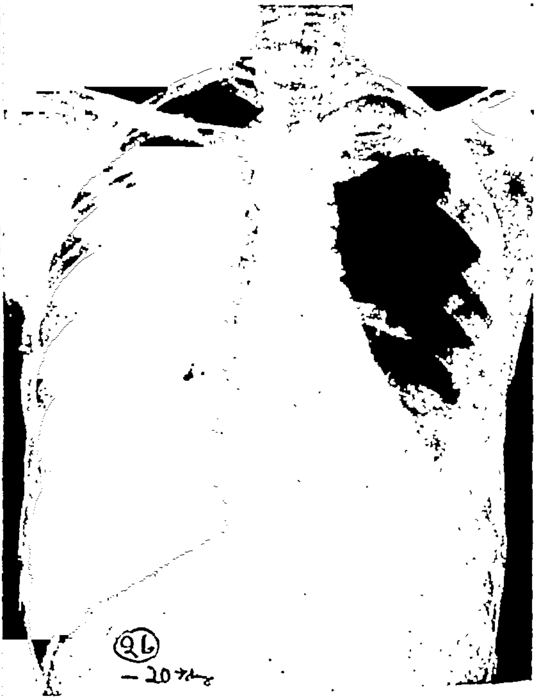

Fig. 4.

Fig. 3 (Patient M.L.).—Roentgenogram of chest taken two days after Streptokinase injection, and following the aspiration of 2,700 c.c. of bloody fluid. There is a noticeable decrease in the size of the density.

Fig. 4 (Patient M.L.).—Posteroanterior roentgenogram of chest on the twentieth hospital day following further aspirations and one day before the second instillation of SK-SD. A striking clearing in the left hemithorax is shown.

At this time ampules of enzyme concentrate, each containing 250,000 units SK and 3,000 units SD were instilled simultaneously in three separate sites. During the next two days 2,700 c.c. of bloody fluid were aspirated (Fig. 3).

The injection was repeated on the twenty-first hospital day with a subsequent yield of 1,145 c.c. over the next three days (Fig. 4).

On Oct. 15, 1949, the thirty-eighth hospital day, a marked improvement had occurred in the physical findings and the x-ray appearance, and the patient was discharged (Fig. 5).

He was studied for pulmonary function Nov. 7, 1949, shortly after discharge from the hospital, which revealed a moderate reduction in ventilation and oxygen uptake on the affected side, especially on exercise.

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*St. Vincent's Hospital, courtesy of Dr. Francis W. Baldwin.

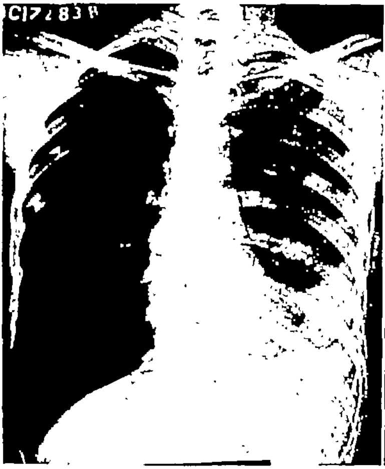

Fig. 5.

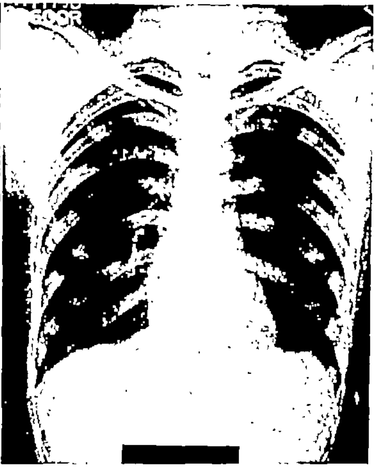

Fig. 6.

Fig. 5 (Patient M.L.).—The appearance of the x-ray photograph at the time the patient was discharged from the hospital. It is to be noted a small residual density remains in the left costophrenic angle. Shortly after this view was taken he had a pulmonary function study at which time a similar roentgenogram was seen.

Fig. 6 (Patient M.L.).—Roentgenogram of chest at follow-up approximately three months following admission to the hospital. There is now complete clearing. Inspiration and expiration films showed definite changes in the level of the diaphragm indicating motion of the diaphragm.

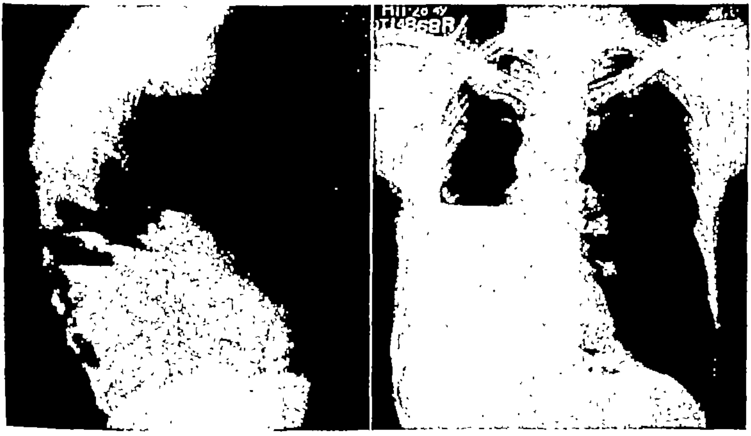

Fig. 7 (Patient D.McG.).—Posteroanterior and right lateral roentgenograms on the forty-fifth postoperative day just before the injection of streptokinase, revealing the loculated hemothorax from which only a few cubic centimeters of bloody fluid could be aspirated.

Subsequent to this study the patient showed marked clearing by x-ray and fluoroscopy examination, with good diaphragm motion and clinical evidence of normal ventilation (Fig. 6). Unfortunately he would not submit to a final bronchospirometric study.

PATIENT D. MCG.—This 62-year-old white man was admitted to Bellevue Hospital with symptoms and x-ray evidence of a neoplasm in the right upper lobe region. Bronchoscopic biopsy disclosed a carcinoma in the right upper left bronchus. On Nov. 4, 1949, a right pneumonectomy was performed with an uneventful postoperative course until the thirty-

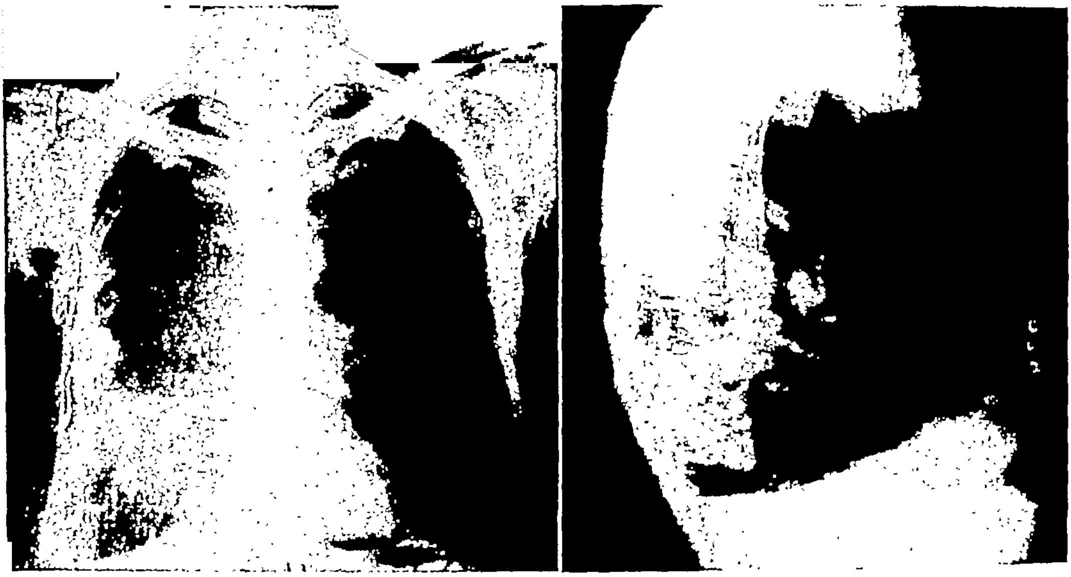

Fig. 8 (Patient D.McG.).—The x-ray appearance following removal of 1,450 c.c. of bloody fluid. There is an area of density remaining in the lower right hemithorax that communicates with the main cavity but there is practically no fluid present.

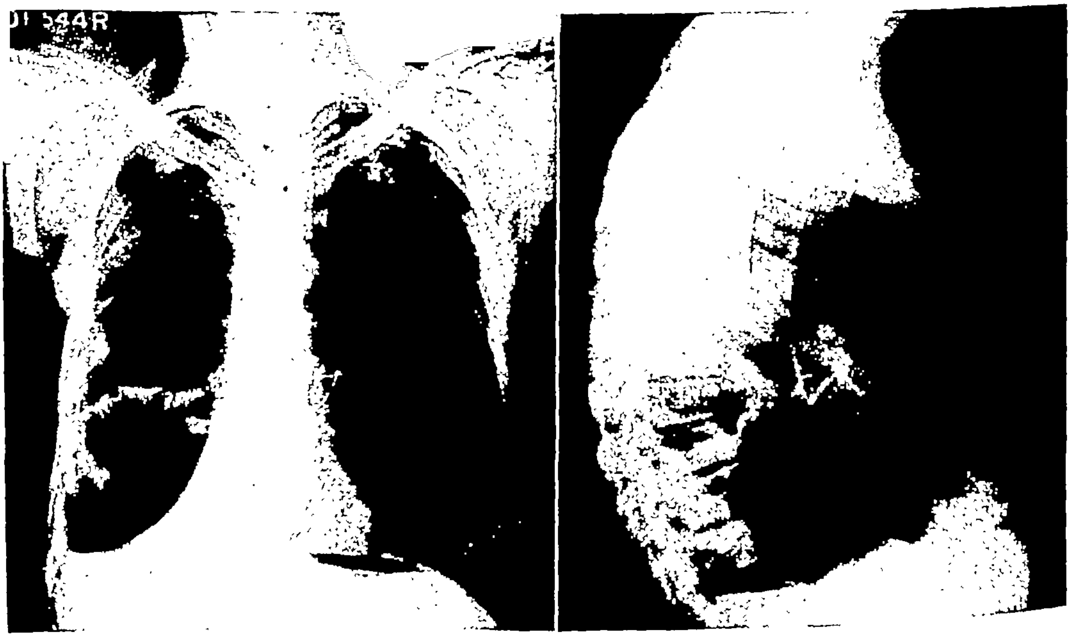

Fig. 9 (Patient D.McG.).—Roentgenograms taken at the end of enzyme therapy following the eradication of the infected hemothorax. It is to be noted that there is further resolution of the density in the lower right chest.

ninth day when his temperature began to range from 101 to 102° F. At this time the roentgenogram showed multiple fluid levels in the right hemothorax and only small quantities of bloody fluid could be aspirated (Fig. 7). The cultures of this fluid were negative for pyogens.

On the forty-fifth postoperative day, because an infected hemothorax was suspected, ampules of SK, 150,000 units, and SD, 60,000 units, were injected into two sites. Twenty-four hours later 800 c.c. of bloody fluid were removed from the right chest and the next day 650 c.c. were obtained (Fig. 8). Each of these specimens cultured out *Escherichia coli*.

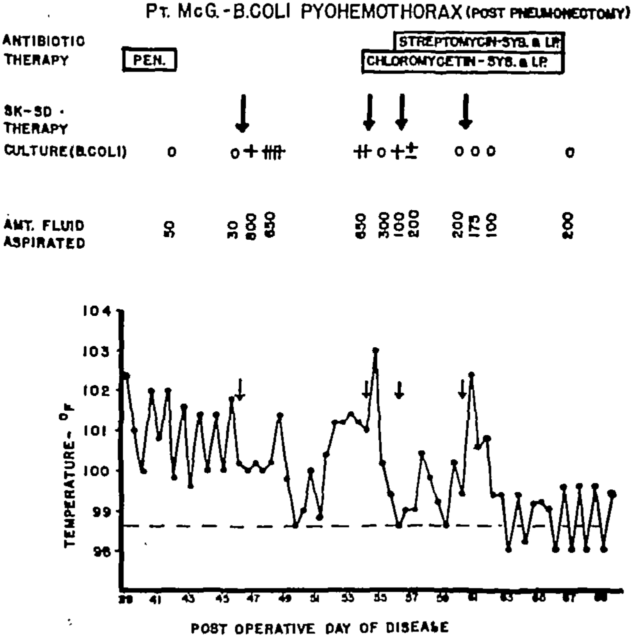

Fig. 10 (Patient D.McG.).—Temperature course, quantitative bacterial cultures, amounts of chest fluid aspirated, periods of antibiotic therapy and the days SK-SD was given (arrows) are illustrated. Note the appearance of *Escherichia coli* after first SK-SD instillation and subsequently its rapid sterilization with combined enzymatic antibiotic therapy.

During the next two days the patient's temperature returned to normal but unfortunately with the intervening holidays the treatment was not pursued and he again became febrile with temperature reaching 103° F. On Dec. 28, 1949 (fifty-third postoperative day), four days following the last aspiration, thoracentesis yielded sanguinopurulent fluid which was still positive for *E. coli* on culture. An injection of enzyme was made then and repeated on alternate days on two subsequent occasions. On the intervening days Chloromycetin and streptomycin were instilled into the chest and at the same time administered systemically. After the third injection of enzyme the cultures were negative and following the fourth instillation of SK-SD his temperature returned to normal and remained there (Fig. 9). Fig. 10 describes the clinical and bacteriological findings in this case. He subsequently underwent two stages of thoracoplasty and has remained free from further evidence of the infection.

DISCUSSION

Whenever blood appears in the thorax there is a good possibility that it will clot despite early attempts at aspiration, and frequently it is permitted to remain unmolested with the hope that it will resolve spontaneously. Large accumulations often defy prompt attempts at complete aspirations as they assume a gel form, and therefore demand more attention than small collections which frequently vanish without any treatment. Massive clotting has been observed four to six hours following trauma[9] and in less time when secondary thoracotomy has been mandatory subsequent to an initial procedure.[10] In such instances aspiration will be of little avail.

Fibroblastic proliferation within a clot, which may appear within five days,[11] leads to organization and this in turn precludes further conservative management. Such evidence should prompt one to evacuate the hemothorax as soon as possible.

Little has been added to the management of hemothorax since the excellent observations of Tuttle, Langston, and Crowley[12] and Samson, Burford, Brewer, and Burbank[13] and others reporting during the war years. These authors suggested that about 15 to 20 per cent of hemothoraces seen in wounds of the thorax progressed to a chronic stage requiring operative treatment, whereas in civilian practice the incidence is more in the neighborhood of 5 to 10 per cent.

Whatever the incidence, the attitude toward significant bloody accumulations should be an aggressive one and every attempt made to evacuate the thorax completely and promptly. With such an approach the necessity of decortication diminishes and the re-establishment of pulmonary function is enhanced. With the addition of SK to his armamentarium the surgeon is offered additional means whereby the management of hemothorax may be accomplished effectively, as illustrated by the results obtained in these cases. Furthermore, when injuries and wounds of the chest occur in large numbers, as in war, the value of these agents will be increased. Striking as was the improvement in the treatment of wounds of the thorax in World War II, the use of streptokinase and streptodornase should lower materially the 15 to 20 per cent of cases of clotted hemothorax already referred to, and so reduce appreciably loss of man power.

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DISCUSSION

DR. E. I. EVANS, Richmond, Va.—We have heard a most scholarly presentation of what will prove to be, I believe, a classical discovery by Tillett and Sherry. I rise simply to add a small amount of emphasis to the presentation of Dr. Read and Dr. Berry; to present two cases, in one of which the results following the use of streptodornase were dramatic and, in the second, to indicate again that with every new preparation given us we have to keep an eye on the patient.

The first patient was a 17-year-old boy who suffered a gunshot wound of the chest about two months prior to coming to us. He came in with the physical appearance of a constricting hemothorax type of chest by all types of physical examination. He was slated for *surgical decortication of the lung, and we prevailed upon Dr. Bigger to be allowed to try* streptokinase on him.

(Slides.) This picture was taken with the patient lying down, Lipiodol instilled into the cavity. The empyema was infected by penicillin-resistant staphylococci. This shows the extent of the cavity which occupied practically the entire left thorax. He was given streptokinase in about the same manner indicated by Dr. Read for exactly twenty days. (Slide.) This shows the appearance of the cavity after six days' treatment. The next slide shows the cavity after twenty-one days' treatment with streptokinase-dornase solution and aspiration eight hours after each injection. The cavity has decreased to a space of only a very few cubic centimeters. The tube is being kept in place until we get practically no drainage. Clinically the boy is well and recovered without surgical decortication of the lung.

The next case is an 8-year-old child who had a small empyema of bloody type following some type of inflammatory pneumonia. Streptokinase-dornase was injected daily, with aspirations eight hours later, and on the sixth day Lipiodol was repeated; we are now confronted with a bronchopleural fistula. I am not sure that we enzymatically removed a covering over an healing bronchus, but this experience indicates that we must reserve final opinion on this treatment. We are impressed in other cases, about six in number (hemothorax following trauma), that streptokinase has been a valuable agent in liquefying a blood clot.

DR. BERRY.—I should like to make public acknowledgment of the generosity of Dr. Tillett and Dr. Sherry in allowing Dr. Read, who has been working with them over the past year, to use some of their own material they had gathered together for presentation. This phase of their work has been done in our chest service and they have been most generous in allowing us to use this outside our own confines whenever such has been necessary. These enzymes doubtless have many other possibilities besides their use in the chest and we have found them of great value on our general service also. I think that the work done here has already proved to us what a valuable agent or pair of agents these two enzymes are in the treatment of empyemas, whether tuberculosis or of pyogenic origin; they are of great help in cleaning them up. We have not yet determined, and Dr. Read may bring that up, what the effect may be upon the healing process, and when we think them safe we use it whenever one is caught in that unfortunate situation of empyema following any resectional work within the chest.

DR. H. A. BRODKIN, Newark, N. J.—I am grateful for the privilege of discussing this valuable paper. I regret that I was not aware that a paper on the subject of streptokinase was to be read and thus failed to bring slides that would have illustrated the value of this agent in the successful conclusion of the following interesting case.

A 21-year-old Negro in the course of a routine chest x-ray examination was found to have a very extensive shadow which resembled a massive pericardial effusion. Numerous attempts at aspiration failed to yield any fluid. After a long period of observation and study, numerous clinicians came to the conclusion that the shadow represented an extremely thickened pericardium, or that the pericardial sac contained a very thick inspissated exudate or fluid. In order to make a definite diagnosis, and because of the possibility that this x-ray shadow might be a large mediastinal tumor, the left chest was explored. A huge, soft, solid tumor, which on microscopic section proved to be a thymoma, was dissected free from the anterior mediastinum. The tumor mass, which extended into both thoracic cavities, was bisected under the sternum. It was found to extend down over the left anterior mediastinum, left costophrenic angle to the vertebral column posteriorly. Its total weight was 1,280 grams. The mediastinum and pleural cavity were drained with two catheters attached to underwater drainage for two days.

Approximately a week later the right anterior chest was opened through an anterior fourth intercostal incision and a similar mass, more extensive, reaching around to the vertebral column on the right, was removed. This mass weighed 1,650 grams, thus making a total of almost 3,000 grams. One of the interesting findings was the presence of a large amount of black clotted blood that spread from underneath the sternum into the left chest, in spite of the drainage tubes. This was removed by means of ring forceps. Two large mushroom catheters attached to underwater drainage were placed into the anterior mediastinum and the right pleural cavity for four days. After the catheters were removed, postoperative films showed an extensive dense shadow which was assumed to be an accumulation of blood. Numerous attempts to aspirate it failed to yield any fluid. The shadow was then assumed to be clotted blood. Some streptokinase was obtained from Dr. Tillett's laboratory, and 10 c.c. were injected into this mass. Twenty-four hours later, aspiration into this mass yielded 500 c.c. of bloody fluid, and the roentgenogram showed almost entire clearing of the mass following aspiration. It was unnecessary to repeat this.

I am sure time will prove that we will owe a great debt to Dr. Tillett and the Bellevue group for furnishing us with this new and extremely valuable adjunct. With the proper use of this agent many surgical chest operations will be avoided.

DR. READ (closing).—I think what Dr. Brodkin brought out as to the usefulness of this material is true. This material is a tool to the surgeon and not the complete therapy in itself in any given situation. It cannot be placed into the chest and forgotten, but should be combined with other practical procedures in the management of the problem. Its action is self-terminating and repeated therapy and aspirations are often required. Its irritative qualities necessitate prompt aspiration within twelve to twenty-four hours, and successive aspirations thereafter. If this plan is not adhered to, exudative elements rich in fibrinogen pour into the area, and may lead to reloculation. With the procedures suggested these irritative effects are minimized, and the desired clinical effect is obtained.

With reference to the bronchopleural fistula: First of all, I think when it is used with the lung in place, in other words, not in a pneumonectomy site but in lobectomy or segmental resection, it is important that a tube should be in the area at the time. If any evidence of leakage or bronchopleural fistula is present, immediate suction is available. There have been two cases come to my attention which have had enzyme therapy following lobectomies, in which bronchopleural fistulas became manifest. As you all know, there is a tamponing effect of debris or fibrin so that a bronchopleural fistula may be dormant or occult. With the dissolution of the coagulum the fistula becomes manifest. This may be avoided in some instances by meticulous pleuralization of the bronchial stump at surgery.

There is no evidence in our studies that the enzymes create bronchopleural fistulas, but only that they make them apparent when they already exist. This is supported by laboratory evidence of complete lack of effect of these enzymes on living cells.

Finally, I should like to re-emphasize that this enzymatic therapy is only an adjunct to the complete management of the patient. For various reasons even decortication might at times be necessary. However, when properly used, it may serve as a very valuable agent in the management of hemothorax and empyema.

THE USE OF STREPTOKINASE-STREPTODORNASE IN THE TREATMENT OF HEMOTHORAX

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THIS article consists of a detailed report of the procedures used and the results obtained following the intrathoracic injections of partially purified streptococcal concentrates containing streptokinase and streptodornase* into patients with massive hemothorax. Previous publications have indicated both the development of the study and also the scope of the applicability of the streptococcal enzymatic substances as a therapeutic measure.[1-8]

The thoracic cases included in this article have been classified on the basis of whether or not the lung had been previously removed by operation or was still in situ. The presence of lung, collapsed by a coagulum, posed the problem of re-expansion and presented other special circumstances associated with the degree of organization of the fibrin, features which were not significant in the handling of the cases of postpneumonectomy hemothorax.

Additional groupings have consisted of cases referred to as *infected hemothorax*. This identification has been given to patients from whom the fluid derived by aspiration was thin and sanguineous rather than thick and purulent, but cultures were either positive prior to therapy or became so following dissolution of the loculated hemorrhagic coagulums.

From the standpoint of enzymatic action the chief basis for the differentiation between infected *hemothorax* and *empyema* is referable to the fact that in the former the principal solid constituent of the exudate is fibrinous against which streptokinase is primarily active, whereas in the latter group desoxyribose nucleoprotein is an additional important increment of the purulent exudate which requires the action of streptodornase.

The results obtained in patients with empyema are given in a separate article.[9]

The first 27 cases of hemothorax, treated with streptococcal enzymes by our group, constitute the substance of this report. They are divided as follows:

1. Sterile postpneumonectomy hemothorax—10 cases.
2. Infected postpneumonectomy hemothorax—4 cases.
3. Sterile hemothorax, traumatic, with lung in situ—11 cases.
4. Infected hemothorax, traumatic, with lung in situ—2 cases.

In assembling the data of each of the groups, the following patients previously reported upon have been included in this report.

Patient A. A. (Table I) was previously reported by Tillett and Sherry;[1] patients A. L. (Table I), H. F. (Table III) by Tillett, Sherry, Christensen,

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From the Department of Medicine, New York University College of Medicine, and the Third Medical and Surgical Divisions of Bellevue Hospital (with special acknowledgments to the Chest Surgical Service, Dr. Frank Berry, Director).

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*Referred to as SK-SD.

Johnson, and Hazlehurst;[6, 7] patient D. McG. (Table II) by Tillett,[8] and was included in the presentation of Read and Berry made at the Thirtieth Annual Meeting of The American Association for Thoracic Surgeons. Their report is a separate communication in this JOURNAL.[10]

MATERIALS AND METHODS

Streptococcal concentrates containing streptokinase and streptodornase have been prepared by methods described by Christensen[11] and modified by Lederle Laboratories, Inc.* to meet practical problems encountered in the large scale production of active material.

Since in clotted hemothorax, fibrin constitutes the major substrate, streptokinase was the more important of the two enzymes employed. In several instances preparations rich only in streptokinase and containing very small amounts of streptodornase were used. These latter preparations were as successful in liquefying sanguineous coagulum as preparations rich also in streptodornase. From the standpoint of enzymatic activity, therefore, the quantitative data will center around the fibrinolytic reaction. However, since as a practical measure of manufacture, SD is usually incorporated in the finished product, the mixtures of SK-SD were used for injection into the patients.

The streptococcal concentrate was supplied in a lyophilized state under which conditions it was found to be sterile and stable. It is readily soluble in water or physiological saline but once put into solution, its potency begins to diminish. The practice has been adopted, therefore, of dissolving the contents of the ampule in physiological saline just prior to its actual introduction into the pleural space.

Dosage: Streptokinase.—The dosage of streptokinase per injection used in this study ranged from 80,000 units to 450,000 units per injection. Theoretically the unit dosage should bear a quantitative relationship to the amount of coagulum present in the thorax. However, since the latter cannot be measured accurately, varying amounts have been used for clinical trial. Doses above 100,000 units of streptokinase routinely set into motion large amounts of the fibrinolytic enzyme system whereas doses under 100,000 units in preliminary studies were not consistent in activating sufficient amounts of the fibrinolytic system for maximum effect in the thoracic area. Where estimations of the total amount of fluid and coagulum can be made, the maximum fibrinolytic systems can be expected to occur with titers of 100 to 500 units of streptokinase per cubic centimeter of chest fluid. For routine purposes in thoracic injections, ampules containing approximately 200,000 units of streptokinase have been regularly employed as a standard dose.

At present the enzyme concentrates used contain an inhibitor to streptokinase that is only of significance in highly concentrated solutions of the enzyme, and is of no significance in dilute solutions.

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*Lederle Laboratories, Inc., Pearl River, N. Y., supplied the preparations used in this study.

Fig. 1 shows the results of an experiment designed to demonstrate this inhibition.* It will be noted from Fig. 1 that maximum speed of fibrinolysis occurred with a 1/32 dilution of the original streptokinase solution.

From a practical standpoint of routine procedure, when a lyophilized ampule of streptokinase of 200,000 to 300,000 units is diluted up into approximately 50 c.c. of saline, or when the ampule is made up in a smaller volume of saline but injected into an area which has enough free fluid to dilute out the inhibitor, then the streptokinase will be maximally active. However, if one were to dilute up the whole dose in 1 to 2 c.c. of saline and inject it into the center of the coagulum in which no fluid was available to serve as diluent, little fibrin lysis would occur.

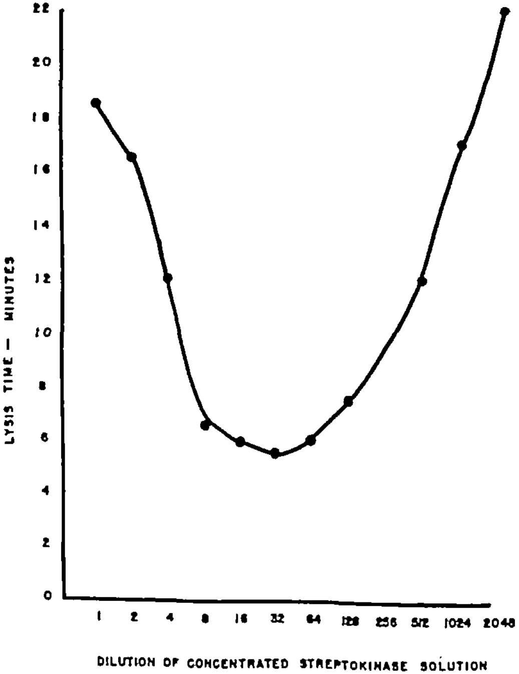

Fig. 1.—Demonstration of an inhibitor in a streptokinase preparation. Inhibition of fibrinolysis is evident at the highest concentrations of the streptokinase solution. Fibrinolysis is maximal at a 1/32 dilution of the solution.

Two and possibly three types of inhibition of the fibrinolytic system are present in normal serum and in sanguineous exudates. One has been referred to as *trypsin inhibitor*[2] *and antifibrinolysin.*[12] Our studies demonstrated its presence in a uniform amount in all specimens. Its action has not introduced difficulties in practical therapy. Whether or not the trypsin inhibitor and antifibrinolysin are the same or different substances remains to be determined.

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*A purified streptococcal concentrate containing 300,000 units of streptokinase was dissolved in 10 c.c. of 0.01 M saline phosphate buffer at pH 7.4. To 0.1 c.c. of serial dilutions of this preparation was added 0.1 c.c. of a 1 per cent solution of Human Plasma Fraction III (source of serum increment), 0.1 c.c. of a 1/3 dilution of Hemostatic Globulin (Lederle) (thrombin), and 0.8 c.c. of a 0.25 per cent Bovine Fibrinogen solution. Time of lysis of the resultant clot was measured.

A specific antibody to the streptococcal product has been described as occurring following both acute hemolytic streptococcal infections,[13] and the injections of SK.[2] Recognition of its presence is important only in patients who required protracted treatment. When present its inactivating effect has been overcome by increasing the dosage of SK one- or twofold.

Summary of Data Pertinent to Streptococcal Fibrinolysis in Relation to the Treatment of Patients.—All of the laboratory measurements previously described,[1, 2] which served as the experimental background in which the use of enzymatic therapy in patients was developed, are not regularly necessary for the practical and effective clinical application of streptokinase in treatment except for special instances.

However, for purposes of immediate reference, the increments involved in the fibrinolytic system and the mechanism of action are recapitulated in a brief review and are illustrated by the findings obtained from a case of clotted hemothorax presented in Fig. 2.

Streptokinase (SK) is elaborated extracellularly by hemolytic streptococci[14] and this product mediates and promotes the rapid alteration of fibrin and fibrinogen in an enzymatic system which requires the presence of a serum factor present in normal human blood.

The serum factor (lysing factor of Milstone,[15] plasminogen of Christensen and MacLeod,[16] and serum pro-fibrinolysin of Loomis[17]) occurs naturally in human blood in a stable but *inactive* form, and is referred to by us as the *activatable fibrin lysing system,* since it awaits the addition of streptokinase in order to exhibit the total qualities of active, rapidly acting, fibrinolysis and fibrinogenolysis. The *active fibrin lysing system,* when formed, is labile. The duration of its action, both in vitro, and in vivo, in patients, is self-terminating.

The patient A. Mc. (Fig. 2 and also Table I) was a 50-year-old white man who developed a loculated hemothorax following pneumonectomy for tuberculosis.

From the data of Fig. 2 note that the injection of streptokinase has rapidly activated large amounts of the active fibrin lysing system at the expense of the serum precursor (activatable fibrin lysing system) which was present in the exudate in an amount equal to that normally present in circulating blood. In our experience in the study of sanguineous exudates in patients, the active fibrin lysing which appears promptly following the introduction of the streptococcal product, has been demonstrable only *if and when free streptokinase is simultaneously present.* Furthermore, as long as free streptokinase is still demonstrable, continued activation of the fibrinolytic system proceeds, after the first period of activation, according to the extent to which there is a renewed influx locally of new serum increments. When, after the injection, free streptokinase is no longer present, the titer of activatable precursor rises to its previous level as supplied from the exudation of fresh serum and is available for the subsequent development of more fibrinolytic activity. This latter point, therefore, serves as an indicator for the appropriate time to administer the next dose of SK.

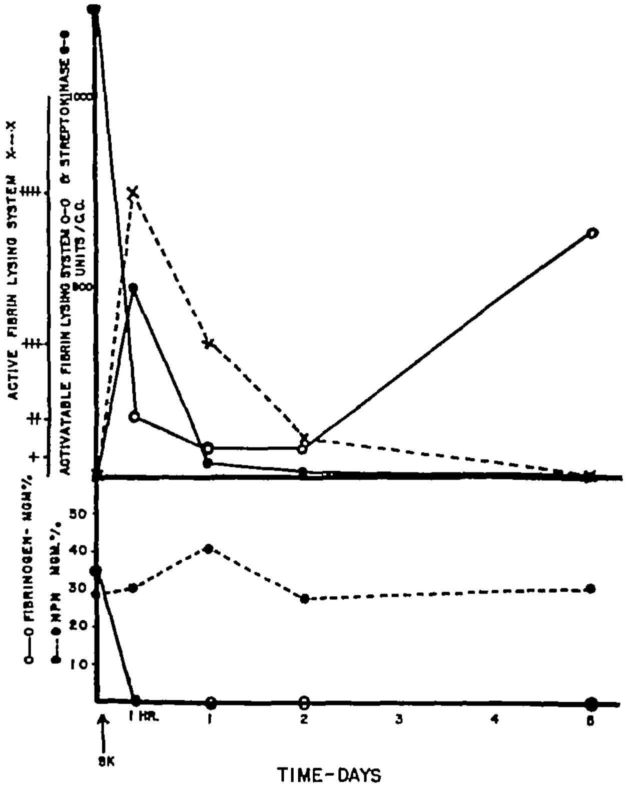

Fig. 2.—Summary of biochemical changes in chest fluid of patient A. Mc. (postpneumonectomy hemothorax) following the intrapleural administration of 300,000 units of streptokinase. Note the activation of the fibrin lysing system (*X—X*, upper graph) at the expense of the activatable precursor (*O—O*, upper graph), and the rapid fibrinogenolysis (*O—O*, lower graph) following the SK injection.

The significance of the serum increment in streptococcal fibrinolysis is well illustrated in the following test, conducted in vitro, with material from a patient.

Tube on the left (Fig. 3) contains a fibrinous mass suspended in 10 c.c. saline containing 10,000 units streptokinase and incubated at 37° C. for 4 hours. No lysis is noted. (The fibrinous mass was removed from the pleural surface of a patient during decortication of a foul empyema.) The tube on the right contains a similar sized fibrinous mass, from the same patient, suspended in 10 c.c. serosanguineous fluid containing the normal amount of lysing factor to which 10,000 units streptokinase was added and incubated at 37° C. for 4 hours. Complete lysis of the fibrin has occurred. The serosanguineous fluid was removed by aspiration from the pleural cavity of a patient with hemothorax. The patient from whom the fibrinous specimen used in the preceding test was obtained had not been treated with SK-SD, nor was a sample of pleural effusion from this patient tested for serum lysing factor. Up to the present time a deficiency of the serum lysing factor in pretreatment samples of exudate has not been observed except in rare instances.

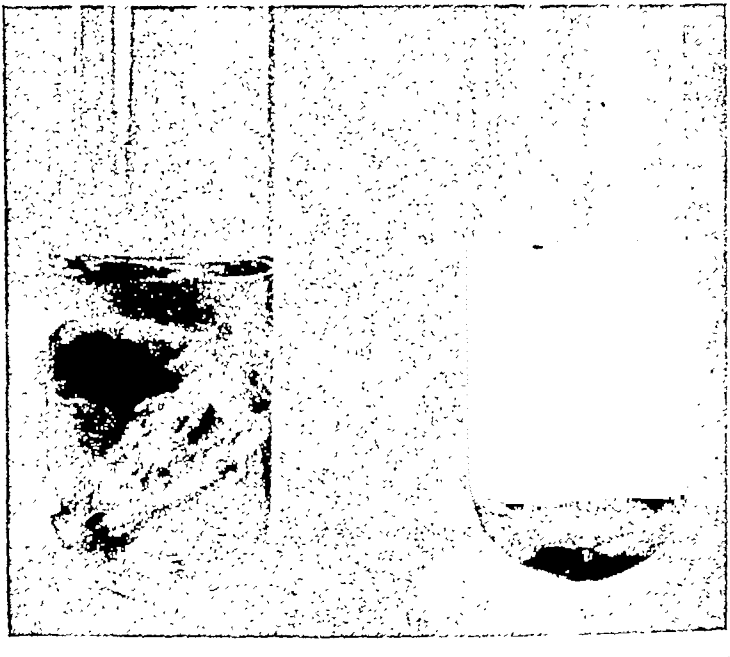

Fig. 3.—Demonstration of requirement of combination of streptokinase-serum factor to effect fibrinolysis (see text).

For practical purposes in following the course of events in the treatment of patients, and in association with clinical observations, determinations of the *active fibrin lysing system* present in the sanguineous exudate has proved to be the most useful of all the tests mentioned. It is performed as follows:

Active fibrin lysing system (equivalent to plasmin). To 0.1 c.c. samples of chest fluid are added 0.9 c.c. of 0.25 per cent Bovine Fibrinogen (Armour) in 0.01 M saline phosphate buffer (pH 7.4); 0.1 ml. of thrombin solution* is then rapidly added. The tubes are incubated in a water bath at 37° C; 0.1 ml. of saline instead of chest fluid is used as a control. The time of complete lysis of the fibrin clot is noted. In this method, the lysis of a standard fibrin clot by a fixed increment of body fluid is graded + to ++++, as follows:

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*In the method originally described for active fibrin lysing system,[1] Lederle's Hemostatic Globulin was employed. This material is no longer available. Parke-Davis Bovine Thrombin containing 5,000 NIH units in a lyophilized ampule is now employed. (The ampule is diluted up in 50 c.c. of 50 per cent glycerol and stored in the icebox; 0.1 c.c. aliquots are employed for clotting test fibrinogen solutions.) However, this preparation contains a small amount of active fibrinolytic enzyme and has necessitated setting up different time standards relative to the control for expressing active fibrin lysing enzyme titers.

Lysis up to 1 hour	++++
Lysis 1 to 3 hours	+++
Lysis 3 to 6 hours	++
Lysis 6 to 8 hours*	+
Control: 8 to 24 hours spontaneously	

This represents a practical method of expression of the concentration of the fibrin lysing enzyme. It is also of importance to note that whereas a unit of plasmin[2] is based on the liquefaction of a standard amount of fibrin in ten minutes, the estimations of the fibrin lysing system take into account the total time during which fibrinolysis is occurring. The significance of the time factor is not only important in in vitro studies but is obviously of special significance in gauging the utilization of SK in patients according to the principle of obtaining maximum effect from a single dose which may proceed as long as 24 hours.

An active fibrin lysing system should be present in significant amounts (at least ++) and demonstrable by this method for periods up to 24 hours following the intrapleural injections of streptokinase. This test need not be routinely employed but reserved for cases in which satisfactory fibrinolysis does not take place.

Method of Handling Individual Treatment.—Streptokinase, when injected, puts into operation immediately the process of fibrinolysis, which continues in the thorax for approximately 24 hours and then becomes self-terminating.

Although the streptokinase, when injected, immediately activates the fibrin lysing system, extensive lysis of the coagulum in the chest and the dissolution of fibrin loculation occur at variable periods of time depending on the physical form of the coagulum and the extent of contact between enzyme and substrate. (For discussion of this point see reference 8.) We have adopted a policy, therefore, of injecting the solution of SK and leaving it in situ for 12 to 24 hours before tapping the area again. After this period of time the complete removal of all fluid should be accomplished, by multiple thoracenteses if necessary (though the latter is rarely necessary). Extensive aspiration is of special importance because (1) it permits immediate radiographic examination to determine *what has been accomplished as evidenced by changes in the x-ray* shadow and increased expansion of the lung, and whether or not further therapy is necessary, (2) it removes from the chest residual irritants and pyrogens associated with the concentrates and the breakdown products of enzymatic digestion. If the lysed fluid is not aspirated, it not only prevents the expansion of the underlying lung, but may act as the site of new clotting and loculation when the enzyme action is finished, and new increments of fibrinogen enter from the pleural surface.

In an optimally successful situation following one injection, the complete coagulum is liquefied and removed within 24 hours by aspiration (usually 14 to 16 hours after SK). Further exudation of fluid due to the local irritating effect of the treatment usually appears in decreasing amounts over the next 24 to 48 hours and is removed by aspiration leaving the space clear. When fluid continues to exude in large amounts after this period of time, the reaccumulation has been found to be related to the underlying pathology rather than the use of the streptococcal enzymes.

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*Or faster than control.

Number of Treatments.—If complete liquefaction of the coagulum is not accomplished with the first injection, repeated injections may be indicated at 48-hour intervals, and should be continued until a maximum effect has been obtained. The routine procedure has been adopted, therefore, of administering SK on alternate days and draining by aspiration on alternate days.

The need for subsequent injections may be gauged by whether (a) a satisfactory clinical result has already been accomplished, (b) the fluid removed at aspiration has lost all its sanguinity and has been replaced by a thin serous fluid, (c) no more fluid can be obtained by aspiration.

Since streptokinase depletes the activatable fibrin lysing system in the chest fluid, subsequent injections of streptokinase do not set in motion as active a fibrin dissolving system as the initial injection. This may be a limiting factor in obtaining as extensive a fibrin dissolution on subsequent injections as occurs with the first injection, particularly if repetitions of treatment into large areas were to be given once or twice daily instead of at the spaced intervals described previously.

Toxicity.—The toxic reactions, described in detail in reference 8, are chiefly limited to a pyrogenic one and a local outpouring of serum and leucocytes. The febrile response, occurring in 60 to 70 per cent of cases, begins about 6 hours after the injection, reaches its peak (averaging 3° F.) in 24 hours, and subsides during the ensuing 24 to 48 hours. We have never observed it as a serious reaction, although it is our impression that febrile responses occur more frequently following the lysis of frankly hemorrhagic material than purulent exudates and may in part be referable to the absorption of hemoglobin. The administration of amidopyrine (0.1 Gm. three times daily) on the day preceding and the day of treatment has abolished the thermal reaction and abated considerably the symptomatology. Aspirin has proved useful but less successful than amidopyrine.

CLINICAL RESULTS

Group 1. Sterile Postpneumonectomy Hemothorax (10 cases).—Table I contains pertinent data with respect to the 10 patients of this group and Fig. 4 illustrates by x-ray photographs the extensive liquefaction and removal of the previously loculated coagulum within 24 hours of the instillation of SK.

Comment: It is not the purpose of this article to discuss or recommend the total management of cases of pneumonectomy that may have varying amounts of postoperative bleeding and may present varying surgical anatomical situations that require individualized treatment to obtain optimum objectives after the lung has been removed. The effectiveness of enzymatic fibrinolysis in the cases of Group 1 has been unusually uniform both in the completeness with

TABLE I. CASES OF GROUP 1: UNINFECTED POSTPNEUMONECTOMY HEMOTHORAX*

PATIENT	AGE IN YEARS (SEX)	OPERATION	DURATION PRIOR TO SK (DAYS)	AMT. OF FL. ASP. JUST PRIOR TO SK (C.C.)	AMT. OF FL. ASP. WITHIN 24 HOURS POST SK (C.C.)	TOTAL FL. ASP. POST SK (C.C.)	NUMBER DAYS POST SK ASP.†	SUBSEQUENT COURSE
A. A.	20 (M)	Pneumonectomy for bronchiectasis	29	2	1,100	1,800	12	Febrile course subsided post SK. Thoracoplasty 3 weeks later
H. S.	40 (M)	Pleuropneumonectomy for lung abscess, chronic empyema	14	30	930	1,025	5	Bronchopleural fistula opened and spontaneously closed. Thoracoplasty 18 days later (see text)
A. Mc.	46 (M)	Pleuropneumonectomy for tbc.	17	2	800	1,250	5	Thoracoplasty 4 weeks later
A. L.	31 (F)	Pleuropneumonectomy for tbc.	27	50	630	1,075	8	Thoracoplasty 17 days later. Patient succumbed to pulmonary edema on operative day
F. M.	33 (M)	Pleuropneumonectomy for tbc.	34	30	400	700	3	Thoracoplasty 2 weeks later
M. G.	34 (M)	Pleuropneumonectomy for tbc.	37	0	190	190	1	Tube drainage. Thoracoplasty 3½ weeks later
L. H.	29 (M)	Pleuropneumonectomy for tbc.	40	30	750	1,100	4	*Thoracoplasty 3 weeks later*
F. B.	34 (F)	Pneumonectomy for tbc.	20	25	450	1,230	8	Thoracoplasty 26 days later. Toxic reaction to SK (fever, vomiting)
R. P.	48 (M)	Pneumonectomy for tbc	16	15	900	1,450	5	Thoracoplasty 3 weeks later
M. W.	44 (M)	Pneumonectomy for tbc	14	10	330	550	3	Thoracoplasty 10 days later

*Each patient received 1 injection of SK except Pt. A.A. who received 3 (see text).

†Indicates in days, time over which aspirations were required following fibrinolysis by SK.

which liquefaction has been accomplished with a single injection and in the rapidity with which the desired result has been obtained. The consistent success in the fibrinolytic aspects of the treatment of this type of massive postpneumonectomy hemothorax is referable to the particularly favorable conditions which exist. The thoracic cage serves as a fixed closed "container" for the fibrin deposits and permits the introduction of solutions of SK under particularly favorable conditions of maximum and sustained contact between enzymatic system and its substrate.

The practical point continually arises in this group of patients, as well as in others with massive extravascular hemorrhagic deposits, concerning the time during the postoperative hemorrhagic period at which SK treatment should be instituted. As indicated in Table I, the postoperative day of injections of SK ranged from the fourteenth to the fortieth. In our series the factor which served as an indication for the use of SK was the increasing formation of coagulum that was not amenable to removal by aspiration. The application of lytic therapy too soon after operation might presumably lead to more bleeding by reopening thinly thrombosed vessels. We have up to the present time never observed this complication but it will be subsequently discussed in more detail. Another possible difficulty arising from the application of SK too early postoperatively involves the opening of the bronchus of the pulmonary stump that has not been adequately pleuralized.

A bronchopleural fistula developed in patient H. S. (Table I and *C* and *D* of Fig. 4). The opening was first demonstrable 4 hours after the introduction of 200,000 units of SK, but closed 24 hours later without evidence of the development of contaminating infection of the pleura. The fistula reappeared 18 days later at the time of thoracoplasty and remained open until a suture observed by bronchoscopy was removed. The fistula then closed promptly and drainage ceased spontaneously. A separate report to be subsequently published will deal with our experience in cases of bronchopleural fistulas, which require special consideration because of the contraindication to the use of SK which may exist.

At the other extreme of the timing of the postoperative use of SK, prolonged delay will render the application of the enzyme ineffective if organization has occurred through the completion of fibrotic cellular infiltration of the coagulum. In our experience this difficulty has not been encountered in the cases of postpneumonectomy. For example, patient L. H. (Table I) received successful lytic therapy 40 days postoperatively. However, as will be discussed later, the time factor in relation to organization of tissues appears to be important in patients with hemothorax in whom the lung is in situ.

The *dosage* of SK in the patients of Group 1 consisted of 100,000 to 400,000 units contained in 20 c.c. of sterile physiological salt solution. A single injection was adequate in the treatment of 9 of the patients. Patient A. A. (Table I) received three injections, two of which were primarily for investigational rather than therapeutic purposes. The sharp increase in the amount of fluid obtained by aspiration during the first 24-hour period after the introduction of SK has regularly been a striking characteristic of the effect of the enzymatic solutions, and is evident from the quantitative data given in Table I. The

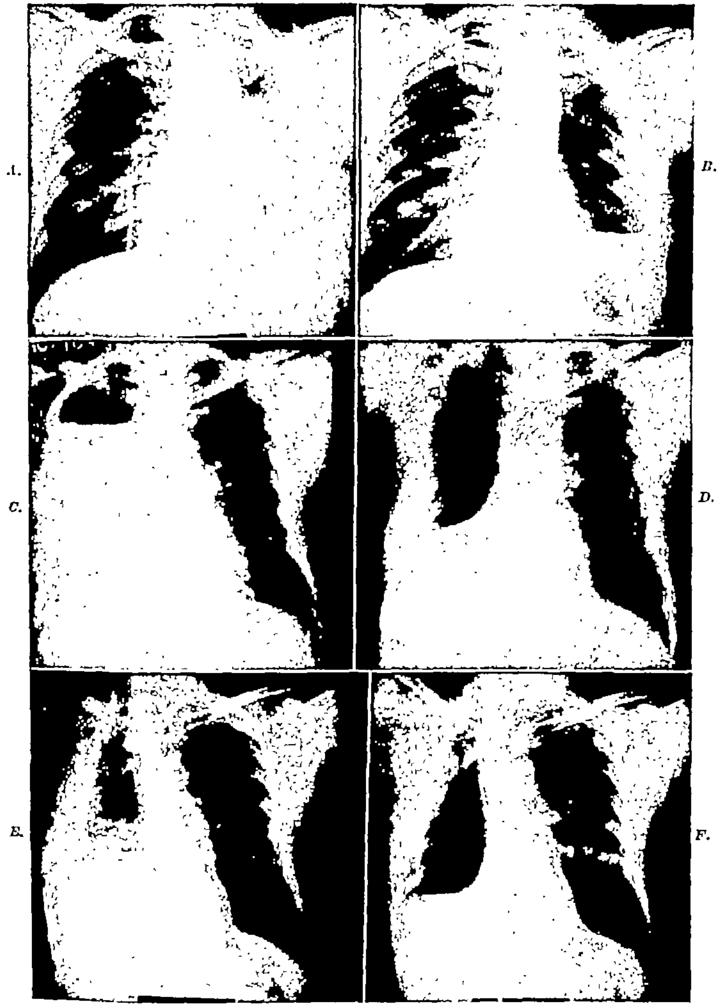


Fig. 4.—Extensive removal of loculated thoracic coagulum, following streptokinase therapy, in three patients with postpneumonectomy hemothorax. *A*, Case L. H., prestreptokinase. *B*, Case L. H., 24 hours poststreptokinase. *C*, Case H. S., prestreptokinase. *D*, Case H. S., 24 hours poststreptokinase. *E*, Case A. Mc., prestreptokinase. *F*, Case A. Mc., 72 hours poststreptokinase.

increase is accounted for by the liquefying process itself supplemented by an outpouring of additional serous material referable to the local irritation.

The subsequent post SK aspirations (Table I) indicate the time required to empty the residual content as an expression of the successful termination of the fibrinolytic purposes of the therapy. In each of the cases of Group 1 thoracoplasty was subsequently performed successfully. In an additional case of our series, previously reported,[8] a marked contralateral mediastinal shift was rapidly rectified following liquefaction and removal of postoperative collections of fluid.

The photographic illustrations in Fig. 4 demonstrate the thoroughness of the lytic action of SK in making possible the ready removal of massive coagulums.

Group 2. Infected Postpneumonectomy Hemothorax (4 cases).—These patients (Table II) have been included in a group referred to as infected hemothorax rather than empyema because, as previously mentioned, at the time they were presented for enzymatic therapy the character of the exudate was that of hemorrhagic coagulum rather than that of purulent infection.

In 1 of the patients (J. H.), cultures of pretreatment samples of the sanguineous fluid obtained by aspiration were positive. In patients R. S., D. McG., and J. R., however, the contaminating organism was recovered only after lysis had been accomplished.

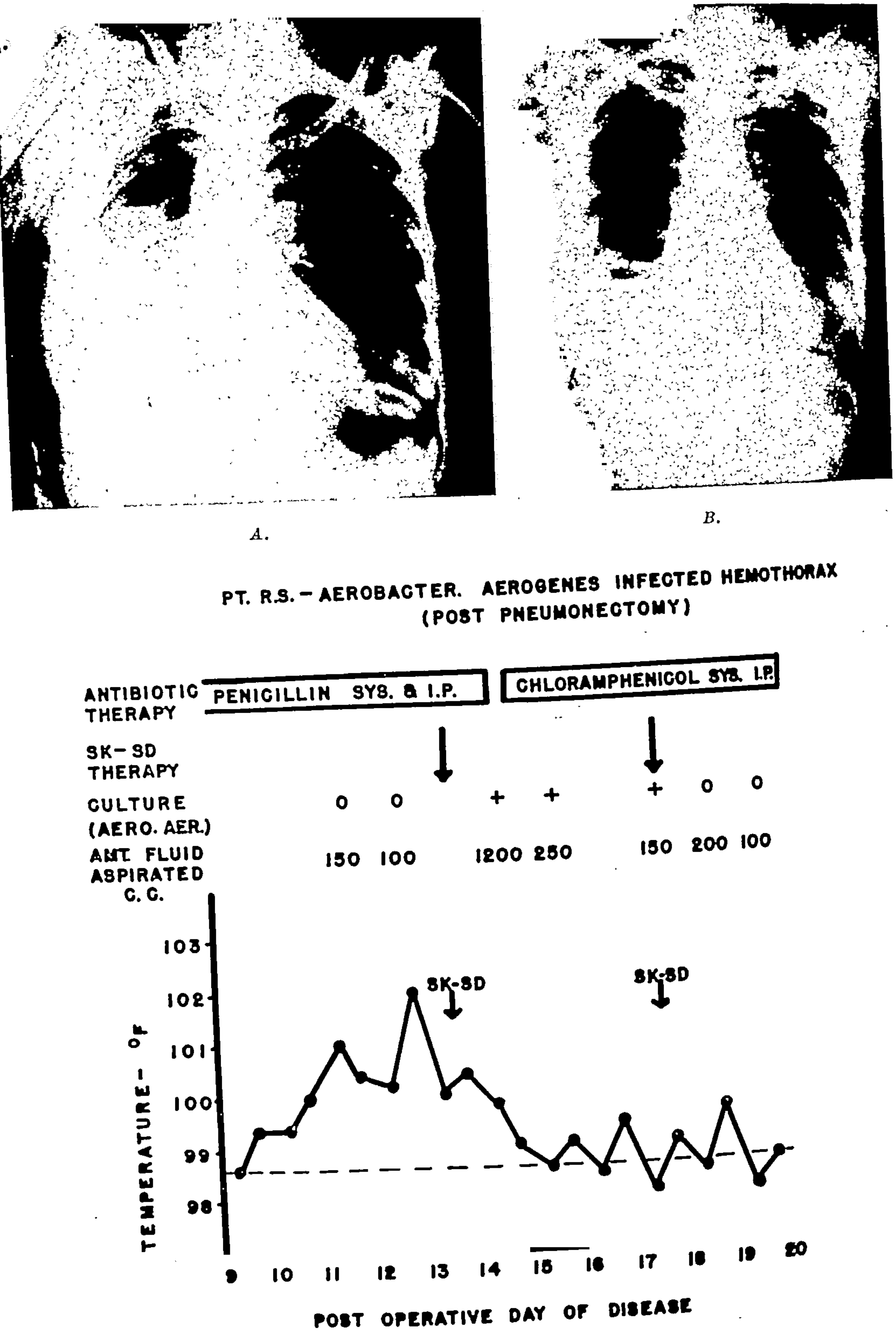
The details of patient R. S. (Fig. 5) are as follows: 57-year-old white woman with chronic lung abscess and suppurative disease of the right lung who had a lobectomy in October, 1949, followed by a pneumonectomy on Feb. 1, 1950. The pathology of the lung removed was described as suppurative bronchiectasis. The patient did well in the immediate postoperative period. The right thorax filled up with a loculated coagulum. On the tenth postoperative day the patient became febrile. Thoracenteses on the eleventh and twelfth postoperative days yielded only 150 c.c. and 100 c.c. of sanguineous fluid, respectively, which were sterile on culture. X-ray examination at this time still revealed an extensive coagulum (Fig. 5). On the thirteenth postoperative day a total of 390,000 units SK and 3,000 units SD were injected intrapleurally in three sites. The next day 1,200 c.c. of thin bloody fluid were removed and the thorax emptied of its coagulum by x-ray examination. Culture of this fluid revealed *Aerobacter aerogenes*. The patient was immediately placed on chloramphenicol per os (2 Gm. every day). Four days later the thorax was again injected with 200,000 units SK and 60,000 units SD in 25 c.c. of a ½ per cent solution of chloramphenicol. By the next day the pleural fluid was sterilized and the infection eradicated. The temperature fell and the subsequent course including thoracoplasty was uneventful. Fig. 5 also graphically summarizes the course of events in this patient.

Patient J. R. (Table II) ran an interesting course characterized by the development of a spiking fever following liquefaction with a single dose of SK-SD (250,000 units). Furthermore, the material aspirated after lysis was positive for tubercle bacilli whereas previous ones had been sterile. Streptomycin therapy was introduced and the fever subsided in 8 days. Cultures of serous exudate which reformed after the primary evacuation were sterile. After an interval of 3 months a thoracoplasty was successfully performed without drainage. There has been an uneventful 2-year follow-up of patient J. R.

Patient J. H. (Table II) (previously reported[6]) was an interesting and instructive example of the capacity for sterilization induced by enzymatic clearing. The intrathoracic coagulum contained *Bacillus pyocyaneus* which, over an extended period of time, was un-

TABLE II. CASES OF GROUP 2: INFECTED POSTPNEUMONECTOMY HEMOTHORAX

PATIENT	AGE IN YEARS (SEX)	OPERATION (PNEUMONECTOMY FOR)	BACTERIOLOGY	DURATION PRIOR TO SK (DAYS)	AMT. OF FL. ASP. JUST PRIOR TO SK (C.C.)	NUMBER OF INJECTIONS OF SK	TOTAL FL. ASP. POST SK (C.C.) (DAYS OF ASP.)	ANTIBIOTIC	SUBSEQUENT COURSE
D. McG.	62 (M)	Ca. of lung	*Bacterium coli*	45	10	4	2,000 (21 days)	Chloromycetin, streptomycin	Sterile and afebrile in 12 days; thoracoplasty without drainage
R. S.	59 (F)	Chronic suppurative disease	*Aerobacter aerogenes*	13	100	2	1,800 (7 days)	Chloromycetin	Sterile and afebrile in 5 days; thoracoplasty without drainage
J. H.	62 (M)	Chronic lung abscess	*Bacillus pyocyaneus*	30	30	5	1,570	None (see text)	Sterile and afebrile in 6 days, thoracoplasty without drainage
J. R.	14 (M)	Tbc.	Tbc.	32	3	1	1,700 (17 days)	Streptomycin	Afebrile in 8 days; thoracoplasty without drainage



C.

Fig. 5.—Case R. S. Removal of loculated coagulum and sterilization of area in a case of infected postpneumonectomy hemothorax. *A*, prestreptokinase. *B*, 24 hours poststreptokinase. *C*, Graphic summary of clinical course.

affected by numerous antibiotic and antiseptic reagents introduced locally. However, following three injections of SK-SD on alternate days, followed by alternate days of drainage, sterilization was accomplished. This sequence of events has been repeatedly observed in other types of refractory infections. The principles involved have been extensively discussed in reference 8.

Comment: Effective lysis was accomplished in the 4 patients of Group 2 as in those of Group 1. However, the presence of viable bacteria introduced a second objective to treatment in addition to the mechanical liquefaction of fibrin.

That the action of the enzymes previously referred to as streptococcal enzymatic débridement[6] has in some instances been followed by the sterilization of areas of chronic refractory infection has been described and discussed.[8]

It has also been made clear that the advantageous use of antibiotic therapy has been enhanced by the local enzymatic cleaning process.

Patients D. McG., R. S., and J. R. received antimicrobial therapy during and, for varying periods of time, after instillation of SK.

The exudates, although thin and sanguineous before therapy, became thicker and more cellular as the injections proceeded. The change was due in part to the cellular outpouring associated with the irritative action of the enzymes and perhaps also to a transient pleuritis set up by the bacteria released from the interior of the coagulum.

Aspirations over a greater number of days were required for Group 2 than for Group 1, although the end result with final successful thoracoplasty was the same in both groups.

Group 3. Uninfected Hemothorax With Lung In Situ (11 cases).—The cases included in Groups 3 and 4 were primarily of traumatic origin. The data of Table III were assembled in order to consolidate special points. However, there were considerable differences in the conditions presented by the several patients that altered the methods of enzymatic therapy and influenced the final results.

The detailed reports of 3 cases are, therefore, presented which illustrate the types of problems and the practical methods that were employed in attaining ultimate enzymatic eradication of the widespread fibrin deposits.

Patient J. W., hemothorax following bullet wound (Fig. 6).—J. W., a 24-year-old Negro man, was shot in the left chest during an attempted robbery. The bullet entered the seventh intercostal space in the posterior axillary line and lodged posteriorly at about the level of the first thoracic vertebra. The patient entered the hospital in shock, dyspneic and coughing up blood. There was evidence of subcutaneous emphysema over the wound, and signs of fluid in the left chest. X-ray examination revealed a hydropneumothorax on the left, with atelectasis of the left lower lobe.

The hemoptysis stopped spontaneously within 24 hours of admission. The patient was placed on large doses of penicillin. Thoracentesis was attempted without success. On the eighth day of illness another thoracentesis yielded only 33 c.c. of sanguineous fluid, and a subsequent tap was completely unsuccessful. By the eighteenth day, x-ray examination still revealed a considerable coagulum at the left base with some thickening of the interlobar fissure (Fig. 6).

TABLE III. CASES OF GROUP 3. UNINFECTED TRAUMATIC HEMOTHORAX (LUNG IN SITU)

PATIENT	AGE IN YEARS (SEX)	TYPE OF TRAUMA	DURATION PRIOR TO SK (DAYS)	AMT. FL. ASP. JUST PRIOR TO SK (C.C.)	NO. INJ. OF SK (M, MULTIPLE) (S, SINGLE)*	AMT. FL. ASP. WITHIN 24 HOURS OF SK (C.C.)	TOTAL FL. ASP. POST SK (C.C.) (DAYS OF ASP.)	ESTIMATION OF PLEURAL CLEARING (SEE TEXT)†
P. R.	47 (M)	Bullet wound	14	25	2 (M)	850	2,700 (18)	Partial
J. W.	24 (M)	Bullet wound	19	100	1 (S)	600	600 (1)	Extensive
W. R.	24 (M)	Bullet wound	11	350	1 (S)	300	300 (1)	Extensive
E. S.	29 (M)	Stab wound	31	1	1 (S)	215	215 (1)	None
W. S.	20 (M)	Stab wound	8	2	1 (S)	100	200 (2)	None
T. C.	31 (M)	Stab wound	10	30	2 (M)	300	1,080 (6)	Moderate
H. F.	52 (M)	Fractured ribs	22	2	1 (M)	400	Drainage bottle (3)	Extensive
J. F.	63 (F)	Fractured ribs	26	400	1 (S)	400	650 (4)	Extensive
C. McD.	53 (M)	Fractured ribs	22	100	1(M), 1(S)	680	1,850 (8)	Extensive
C. B.	36 (F)	Sympathectomy, second stage	23	50	2 (S)	250	725 (6)	Extensive
S. McK.	37 (M)	Vagotomy	2	0	1(M), 2(S)	710	1,810 (4)	Extensive

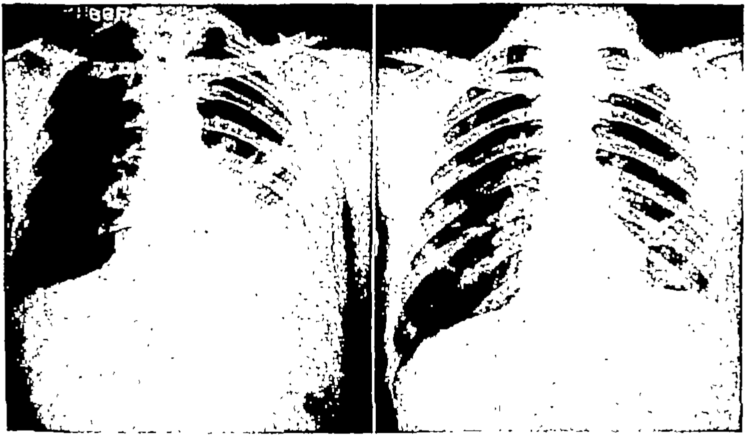
*M signifies simultaneous injection into multiple sites. *S* signifies that total dose was introduced into a single site.

†Indicates prompt effect directly referable to action of SK.

On the nineteenth day the patient was tapped, a small amount of bloody fluid aspirated, and 240,000 units of streptokinase injected. The next day over 600 c.c. of sanguineous fluid were removed with ease. *After this there* was rapid clearing of the area. Fig. 6 was taken approximately 10 days after the use of streptokinase and reveals only a small amount of interlobar thickening remaining. The patient was then discharged to stand trial.

Patient C. B., hemothorax following sympathectomy (Fig. 7).—C. B., a 36-year-old colored woman, entered Bellevue Hospital on Dec. 27, 1948, for her second stage sympathectomy for severe essential hypertension. Surgery was performed on Dec. 29, 1948. Postoperatively the patient developed a hemothorax on the left. Thoracentesis yielded 750 c.c. and 150 c.c., respectively, on the fifth and sixth postoperative days, but subsequent taps were unsuccessful. X-ray examination (Fig. 7) on the twenty-second postoperative day revealed a posterolateral density in the left chest. The patient was injected on two occasions (twenty-third and twenty-ninth postoperative days) with 80,000 units of streptokinase. As a result of the streptokinase, 800 c.c. of sanguineous fluid were removed by thoracentesis with extensive clearing by x-ray examination (Fig. 7). The patient was discharged on the forty-ninth postoperative day, 20 days after the streptokinase therapy.

Patient C. McD., hemothorax due to fractured ribs (Fig. 8).—C. McD., a 53-year-old alcoholic white man, fell down a flight of stairs and sustained fractures of the right frontal bone, nasal bones, outer one-third right clavicle, and multiple fractures of the third to the eleventh ribs on the right. The patient was desperately ill and required transfusions, nasal oxygen, antibiotic, and frequent tracheobronchial suction during the first week of his illness. X-ray examination revealed a hemopneumothorax of considerable extent on the right. By the twenty-fourth hospital day, the patient's general condition had improved considerably but only 250 c.c. of fluid had been previously obtained by two thoracenteses. X-ray films revealed an extensive loculated coagulum in the right chest (Fig. 8, *A*); 240,000 units of SK were injected into the posterior chest and 120,000 units in the mid-axilla; 1,000 c.c. of fluid were removed in the next forty-eight hours with considerable clearing over the posterior chest. However, there was still considerable coagulum in the lower right anterior chest (Fig. 8, *B*). The patient was tapped anteriorly in the fourth interspace just lateral to the nipple, and 240,000 units SK injected intrapleurally. Over the next 48 hours 770 c.c. of fluid were removed from that area. X-ray films now revealed (Fig. 8, *C*) much further clearing and the physical signs of fluid were no longer present. The patient was mobilized, started on deep breathing exercises, and discharged to the clinic. Follow-up x-ray studies (Fig. 8, *D*) 2 months later showed almost complete clearing of the residual density.



A. *B.*

Fig. 6.—Case J. W. Hemothorax following bullet wound. *A*, eighteenth day posttrauma and just prior to streptokinase therapy. *B*, 10 days poststreptokinase therapy.

None of the cases of this group came to decortication and all resolved completely. In 9 of the cases there was extensive lysis of coagulum by injections of streptokinase with removal of large quantities of sanguineous fluid and complete expansion of the underlying lung. Two of these 9 cases were handled by tube drainage, the rest by needle aspiration. In the other 2 cases (E. S. and W. S.) little effect could be attributed to streptokinase. However, in both these cases previous aspirations had removed the major part of the blood since the underlying lung had been almost completely expanded. After streptokinase, small amounts of serous fluid were removed indicating the absence of any sanguineous coagulum. Little immediate effect was noted on the x-ray density, and it is presumed the latter probably represented pleural reaction or complete cellular organization.

Comment: In general the results described in Group 3 have been considered very good but variable when compared to the uniformity of the effectiveness in the cases of postpneumonectomy hemothorax. This is to be expected

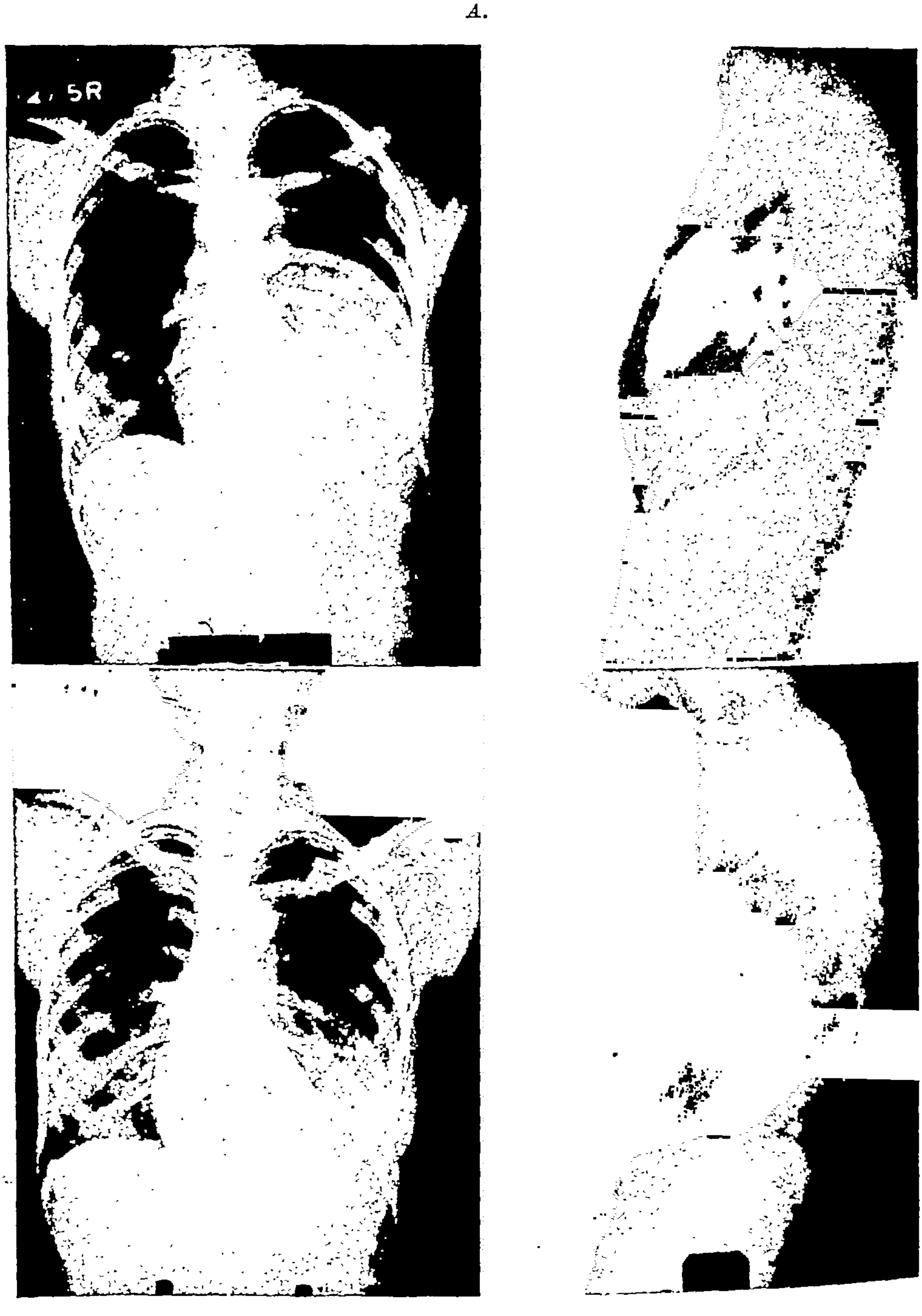


Fig. 7.—Case C. B. Hemothorax following sympathectomy. *A*, Posteroanterior and lateral views on twenty-second postoperative day and immediately prior to streptokinase therapy. Note large hematoma in posterolateral area of left chest. *B*, Posteroanterior and lateral views ten days poststreptokinase therapy. Although some density still remains, extensive clearing is noted on the lateral view.

when recognition is given to the differences existing in the presenting conditions. The hemothorax following pneumonectomy resulted from the slow progressive ooze of serosanguineous fluid into a large thoracic space. Under

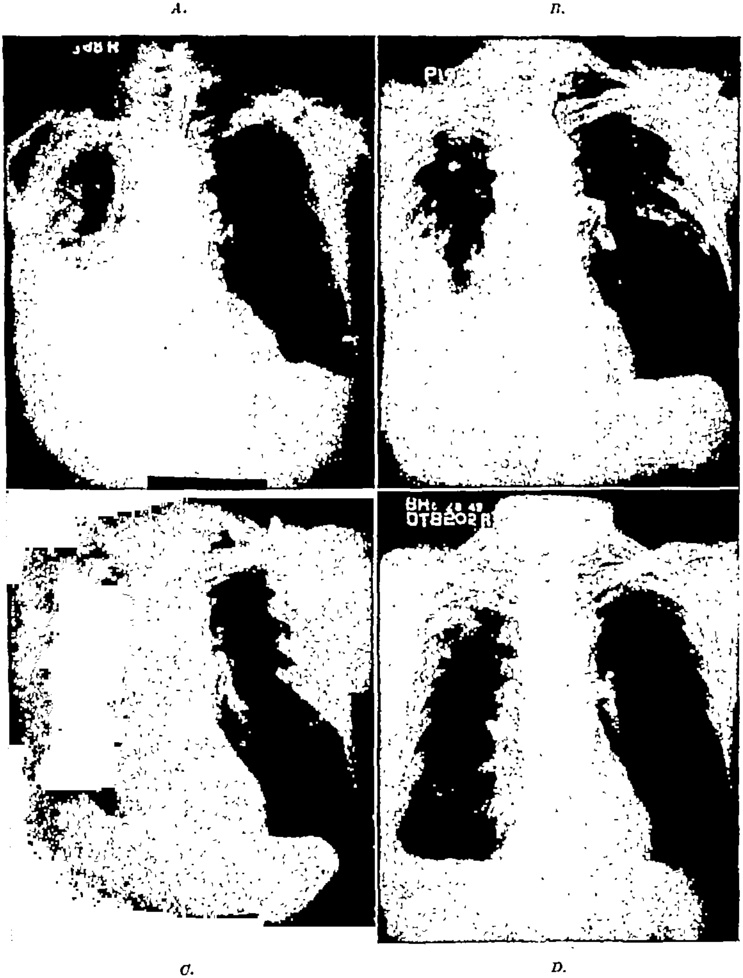


Fig. 8.—Case C. McD. Hemothorax due to fractured ribs. *A*, Appearance on twenty-fourth day posttrauma and immediately prior to SK therapy. *B*, Appearance 48 hours post first SK treatment. *C*, Appearance 48 hours post second SK treatment. *D*, Appearance at follow-up, 2 months post SK therapy.

these circumstances the clot forms gradually and is a meshwork of fluid and fibrin. Organization can begin only from the sole remaining parietal pleura and cannot be expected to bridge across the thorax for a considerable period of time.

In the cases in which hemorrhage occurred into the intact lung-containing thorax, the bleeding, arising from trauma or postoperatively, was usually gross in amount and rapid in rate of initial accumulation. The exudate, being essentially whole blood, is at first rich in fibrinogen and the coagulum formed is liable to be composed chiefly of fibrin. If the lung is still mobile, defibrination may take place with widespread coating of the pleural surfaces with a dense fibrin layer.[18] Melick and Spooner[19] have described the reaction that is evident in the two layers of pleura and have observed that organization begins early from both surfaces and may be completed early according to the closeness of the approximation of visceral and parietal pleura. When extensive pneumothorax has been present together with hemothorax (Patient H. F., Table III), the situation more closely simulates that present in the postpneumonectomy cases, since the collapsed state of the lung causes a wide separation of the visceral and parietal pleural surfaces.

In view, therefore, of our actual experience together with the special conditions inherent in traumatic hemothorax, the principles and practical methods of applying therapy may be outlined as follows:

1. *Institution of SK instillations early following the initial gross hemorrhagic episode but after bleeding has essentially ceased.*

With the exception of S. McK. (Table III) the patients of Group 3 were available for SK therapy *only after* repeated, and often daily, efforts at aspiration by thoracentesis had begun to yield smaller amounts of fluid even though the thoracic shadow seen on x-ray examination remained extensive and the lungs were compressed.

The recommendation of early aggressive treatment as soon as bleeding has spontaneously stopped raises the question, mentioned previously in this article, of whether or not SK will cause recurrence of fresh bleeding. Since the action of SK is a local surface one, it is deemed unlikely that its contact with the one small end of intravascular thrombus would effect its complete liquefaction. In our experience the theoretical improbabilities have been in consonance with actual experience.

Patient S. McK. (Table II) received an injection of SK on the second postoperative day without any fresh bleeding. We have information of 3 other patients at other institutions injected within 48 to 72 hours of the intrapleural bleeding episode without recurrence of hemorrhage.

Patient E. S. (Table III) may be cited as an example of an unsatisfactory result which seems to have been referable to the fact that SK therapy was deferred until the thirty-first posttraumatic day. No liquefying effect was demonstrable either by changes in the character of the fluid or by prompt alterations in the x-ray shadow. It is reasonable to presume that extensive cellular organization had occurred.

2. *Requirements for:* (a) *multiple injections simultaneously into several different sites and* (b) *repeated injections.*

On considering the problems presented by hemothorax with the lung in situ, as experience has accumulated, the value of introducing SK into several different sites at the time of beginning treatment has become evident.

The anatomic situation existing in traumatic hemothorax often consists of an extensive plastering of the pleural surface extending from the extreme posterior limits to the anterior mediastinal area. The extent of the diffusion of the enzyme from a single site contained in 20 c.c. of fluid may be restricted. Since, therefore, lytic action depends on direct contact between enzyme and substrate it is apparent that material placed in the posterior area, for example, may not extend throughout the total pleural area.

In considering the total practical management of patients with massive traumatic hemothorax, the objective is to obtain maximum pulmonary expansion in as short a time as possible. In this connection it is important to recognize the fact that streptokinase serves solely as a reagent which under appropriate conditions causes the transformation of the solid coagulum to a thin solution. Once this effect has been accomplished, the subsequent management of the case, in evacuating thoroughly the pleural contents requires consideration of factors such as desirability of using only intercostal thoracenteses, or closed drainage through a thoracotomy tube with or without negative pressure.

In some instances—not reported in this article—small tears of the lung have previously existed through which positive intrapleural pressure has developed. Similar situations have occurred following SK in postlobectomy cases. In the treatment of cases under these conditions, lysis of clot with SK has been followed immediately by closed tube drainage under water seal and suction has been applied. The pulmonary leaks have closed promptly and improved expansion has been accomplished.

In attempting to arrive at uniformity in the details of the treatment of hemothorax with the lungs in situ, it is obvious that a larger experience with well-studied cases is required. However, that physical changes in the solid fibrin have been effected by fibrinolysis in the patients of Group 3 has been demonstrated.

In attempting to summarize the final results in the cases of Group 3, it has been difficult to measure quantitatively the extent and speed of clearing of the involved pleural area in relation to results that might have been derived from other procedures or from permitting spontaneous absorption to occur.

In spite of this difficulty the following appraisal is offered:

Prompt and extensive clearing of pleural x-ray shadow in 9 of 11 cases.
No effect in 2 cases.

For purposes of completeness in presenting the details of the 10 patients, a brief description of the immediate effects and subsequent course of each is now included.

	IMMEDIATE EFFECT	SUBSEQUENT COURSE
J. W.	Extensive clearing	Discharged 3 weeks post SK with excellent radiographic result.
W. R.	Extensive clearing	Discharged 5 days post-treatment at which time small residual density was continuing to clear.
P. R.	Considerable clearing over upper two-thirds of thorax; residual density in interlobar fissure and at right base.	Almost complete spontaneous resolution of residual density in 5-week period post SK; discharged home.
E. S.	No significant changes noted.	Patient had been previously surgically explored for lacerated lung. At time of injection only straw colored fluid obtained. Extensive clearing occurred spontaneously over subsequent 6 to 8 weeks. X-ray shadow probably pleural and not true coagulum.
W. S.	No significant changes noted.	Patient complicated with prolonged high fever. Only serous fluid obtained after SK. Little effect attributable to SK. Slow clearing spontaneously. Discharged 21 days after SK. No follow-up. Lack of response to SK may be due to pulmonary pathology rather than presence of a coagulum.
T. C.	Extensive clearing over right lower chest posteriorly; moderate clearing over right lower chest anteriorly.	Clinical course complicated by right upper lobe pneumonitis which cleared rapidly with penicillin therapy. Patient discharged 3½ weeks post SK therapy with spontaneous clearing of residual pleural thickening in the region of the diaphragm.
H. F.	Marked expansion of previously collapsed lung, and extensive clearing.	Thoracotomy tube alone had failed in this hemopneumothorax. With SK, coagulum and air evacuated rapidly. Lung completely expanded. Residual density spontaneously cleared. Patient discharged 2 months post SK.
J. F.	Extensive clearing over site of previous shadow with complete expansion of lung. Some residual density anteriorly adjacent to pericardium.	Patient originally considered for decortication by surgeons but severe hypertensive cardiovascular disease contraindicated procedure. Complete spontaneous resolution of small residual density occurred over a 4-week period after SK.
C. McD.	Extensive clearing of multiloculated coagulum. Lung completely expanded. Moderate residual density at site of rib fracture.	Patient complicated by skull fracture and general debility. Surgery contraindicated. Clinical improvement marked after SK therapy. Progressive and complete spontaneous resorption of residual density over subsequent 2 months.
C. B.	Marked clearing over site of previous density.	Small residual density spontaneously cleared over next 2 months.
S. McK.	Good clearing over upper two-thirds of site of disease. Residual density at base.	Although rest of left pulmonary field cleared completely, the density at base remained. This has been identified as an atelectatic left lower lobe, presumably related to the original surgical procedure.

Group 4. Infected Hemothorax With Lung in Situ.—Since the SK treatment of the 2 patients of this group followed the principles previously discussed but varied according to individual condition each may be briefly described as follows without tabulated data:

Patient B. L., white man, 28 years of age, received a bullet wound in the left thorax (Fig. 9). He became available for SK treatment on the thirty-third posttraumatic day, at a time when there had been little or no change in the x-ray shadow covering two-thirds of the right thorax.

The amount of sanguineous fluid aspirated by thoracentesis, increased from 80 c.c. just prior to SK to 800 c.c. within 24 hours after SK. Four lytic treatments were administered of 200,000 units of SK over a 3-week period. There was complete evacuation of the loculated coagulum with expansion of the lung. The hemothorax was infected with *Bacterium coli.* SK treatments were supplemented by Chloromycetin intrapleurally and systemically. The area was sterilized in 3 weeks. There was complete clearing of the diseased area during the subsequent 3 months. The case was complicated by paraplegia and decubitus ulcers secondary to traumatic section of cord.

Patient T. S., white man, 33 years of age, with hemothorax of lower third of left chest which developed following vagotomy performed for peptic ulcer. He became available for SK therapy on the nineteenth postoperative day.

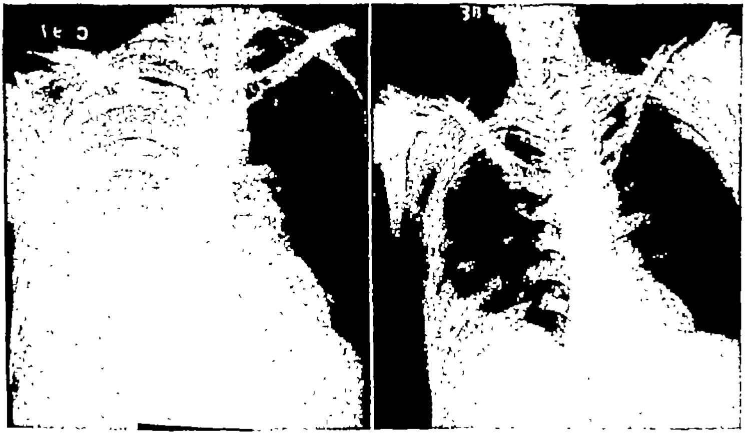


Fig. 9.—Case B. L. Infected hemothorax following bullet wound. *A*, Appearance on thirty-third day following injury and just prior to streptokinase therapy. *B*, Appearance one month later after four streptokinase treatments.

The amount of sanguineous fluid aspirated by thoracentesis increased from 44 c.c. just prior to SK to 325 c.c. within 24 hours after SK. Four lytic treatments were administered of 200,000 units of SK each over 10 days. There was extensive removal of the coagulum. Hemothorax was infected with hemolytic *Staphylococcus aureus.* The organisms persisted in spite of SK and penicillin therapy. The infection cleared following drainage through thoracotomy. During the ensuing 2 to 3 months, there was complete resolution of the diseased area.

It appears justifiable to conclude that in the 2 patients just described, an intractable situation due to clotted infected blood was rapidly and favorably altered following the action of SK which was supplemented by antimicrobial therapy and thoracotomy.

DISCUSSION

The observations on patients described in this report indicate that the intrapleural introduction of streptokinase (occurring in combination with streptodornase) is attended by extensive enzymatic fibrinolysis and liquefaction of hemorrhagic coagulums. In accordance with the details of the methods described, the clinical results have been accomplished, without undue difficulties either immediate or late, and the action of the enzymes has favorably altered the course of many of the patients.

It should be recognized that as a therapeutic reagent, streptokinase acts *solely as a means of effecting fibrinolysis* and, in many cases, serves only as an adjunct to the broad management of hemothorax that may involve essential physiological and anatomical principles inherent in intrathoracic problems.

Further studies on the use of streptokinase are required in order to extend its clinical usages, to define more clearly the best methods of application, and to determine the degree to which its action may obviate or simplify other more difficult procedures.

SUMMARY

1. In 10 patients with massive sterile postpneumonectomy hemothorax, *the injection of solutions of streptokinase-streptodornase* was uniformly effective in liquefying rapidly the intrathoracic coagulum and affording its removal by aspiration.

2. Four patients with infection contained within the postpneumonectomy hemothorax were treated successfully in a similar manner, appropriately supplemented by the use of antibiotic reagents.

3. Eleven patients with traumatic hemothorax (bullet wound, stab wound, fractured ribs, and postoperative) with lungs in situ, have been treated by injections of the enzymes, often introduced simultaneously into multiple sites.

In 9 of the patients fibrinolysis was followed by a marked increase in the amount of sanguineous fluid removed by aspiration and extensive clearing of the pleural area.

4. In 2 patients with infected traumatic hemothorax an intractable state was rapidly and favorably altered by the use of streptokinase-streptodornase and was followed by recovery.

5. Details *of the mechanism of the action of the* streptococcal fibrinolytic principle have been reviewed and the practical aspects of its use have been described in detail.

The authors are indebted to Mr. John P. Goeller for the excellence of the photographs reproduced in this article, as well as for many other macro- and microphotographs he has supplied.

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PULMONARY PARAFFINOMA (LIPOID PNEUMONIA)

A CRITICAL STUDY

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THE wide spectrum of pulmonary infiltrates so long a problem to both radiologist and clinician is gradually being banded off and focused into recognizable segments.

Pulmonary paraffinoma, which is advanced lipoid pneumonia due to mineral oil, still continues to masquerade and elude diagnosis. We wish to emphasize that pulmonary paraffinoma can mimic lung cancer clinically, radiographically, grossly at the operating table, and is even mistakenly called cancer on frozen section. This mistake has been made by us and reported by others.

Laughlin's[1] report in 1925 on lipoid pneumonia in four infants and one adult was the first description of the disease in man and stimulated great interest. Pinkerton two years later reported six cases of lipoid pneumonia and for the first time presented a clear account of the pathologic events occurring after mineral oil reaches the pulmonary alveolus.

Ikeda,[2] in 1937, made the observation that lipoid pneumonia seen in infants differs pathologically from the usual lesion in the adult. Recognizing the tumorlike character of the advanced adult type lesion, he gave it the descriptive title paraffinoma.

Despite these early clear-cut descriptions, there has been a tendency in both the literature and practice toward a confusion of terms and meanings concerning lipoid pneumonia. The present study comprising a critical analysis of our own cases and an extensive review of the literature represents an effort on our part to define a clinical and radiographic picture which can be fairly consistently recognized. We have been fortunate in having the help of Pinkerton in this study, and he has personally reviewed all the sections in our own series.

The infantile type of lipoid pneumonia which is due to a variety of lipids is not as frequently seen by the thoracic surgeon as is the adult type. Goodwin's[3] excellent summary of the clinical picture of this disease stressed that the baby is either one suffering from a neurologic lesion resulting in loss of consciousness, absent cough reflex, or requiring tube feedings, or is debilitated and has been given oil medication. The child coughs, has rapid respirations, and fails to gain weight. Radiographically, infantile lipoid pneumonia exhibits infiltration in aspiration areas which persist unchanged for months. Lack of hilar adenopathy is a major point in differentiating the lesion from tuberculosis. The usual accentuation of bronchial markings seen in chronic inflammatory lesions is strikingly absent; there is little pleural reaction.

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The infantile type of lipoid pneumonia due to mineral oil represents temporally the initial stage of the adult type and consists of a process in which alveoli are occupied by oil-filled macrophages and free oil globules. The lesion is usually more extensive than the adult type and unaccompanied by the late changes of fibrosis and granuloma formation.

The adult type of lesion, with which we are chiefly concerned, usually occurs in older individuals who are habitual users of mineral oil orally, intranasally, or intratracheally. Neurogenic and mechanical interference to swallowing may be a factor, but is by no means always present. Mineral oil as such or in one of its medicated forms is the sole etiological agent. *There may be no pulmonary* symptoms or there may be such symptoms as chronic cough with or without sputum, hemoptyses, low-grade fever, frequent lower respiratory infections, and dyspnea on exertion. When compared with the minimal symptoms presented by the patient, the gross roentgenologic findings are usually strikingly greater than would be anticipated. Clinically and radiographically, the lesion is most often interpreted as a primary or metastatic tumor, or an unresolved pneumonia.

Radiographically, a pulmonary paraffinoma appears as a rather homogeneous *shadow with sharply defined peripheral limits and a contrasting feathering* of density at its hilar aspect; this latter point we feel is a particularly valuable diagnostic sign. This correlates well with the pathogenesis of the lesion, namely, the macrophage transport of the oil to the hilar lymph nodes along the peribronchial lymphatics. The lesion is located in recognized aspiration sites in greatest frequency, for example, lower lobes, apical divisions of lower lobes, and subapical segments of upper lobes. In other words, the lesion is segmental in location. Hilar adenopathy as seen in advanced carcinomas has never been recorded or observed by us. The shadows are permanent and incapable of significant resolution. The lesions are often multiple and are often bilateral. The resemblance to the shadows cast by tumors is marked.

For an understanding of the pathologic picture of the lesions of lipoid pneumonia we are indebted chiefly to Pinkerton[4] and the following description is drawn in part from his studies. First of all, the pulmonary pathology varies with the type of oil and the length of time it has been in the lung. This explains the difference between the infantile and adult types. Pathologically, pulmonary paraffinoma represents a late stage of granulomatous productive inflammation, often clearly localized, densely fibrous and neoplastic in appearance. Mineral oil is inert and acts purely as a foreign body in pulmonary tissues. Elimination from the lung occurs by two methods: (1) expectoration and (2) transport to regional lymphatics in phagocytic cells.

Early, the adult type of lipoid pneumonia grossly resembles the gray hepatization stage of lobar pneumonia. The older adult type lesion or paraffinoma consists of one or a group of nodular masses of varying size lying in close proximity to major bronchial trunks. The mass is sharply demarcated from adjacent lung parenchyma in its periphery. The overlying pleura may be thickened and puckered. The mass is firm, and the cut surface is mottled yellow to grayish-yellow. Small cavities filled with oil are seen and the entire cut surface is oily. Its center is made up of a lobar or lobular bronchus.

A lesion is acceptable as a paraffinoma when the histologic picture described is found and the presence of mineral oil is demonstrated by positive staining with Sudan red and absence of staining with osmic acid. The failure of mineral oil to stain with osmic acid was first pointed out by Pinkerton.[4] Extraction of oil chemically, saponification tests, iodine numbers, and fluorescence tests are not necessary for establishing the diagnosis.[5]

In 1943, Wood[6] reported a case of bilateral alveolar cell carcinoma of the lung associated with lipoid pneumonia due to mineral oil. He attempted to establish an etiological relationship between lipoid pneumonia and the development of carcinoma. He quoted Twort and Lyth[7] who had found that several fractions of natural mineral oil produced primary lung tumors in mice. Wood compared his case with Jagziekte of sheep. One of our cases of pulmonary paraffinoma, or adult type lipoid pneumonia, exhibited epithelial proliferations of such a degree that a frozen section diagnosis of cancer of the lung was made. This epithelial proliferation was noted in the experiments of Pinkerton.[4] Sante[5] reported two cases of squamous carcinoma of the lung occurring with lipoid pneumonia. The carcinoma arose within the lesion in one of the two cases. Microscopic sections were interpreted as showing carcinoma plus lipoid pneumonia. The regional nodes contained no cancer.

Eleven authors[2, 8-14] writing from 1933 until December, 1949, have reported adult type lesions which were tumorlike in their clinical aspects. Janes[14] of this association reported two cases in October, 1947.

CASE REPORTS

CASE 1 (B. A.).—This 61-year-old white woman entered Barnes Hospital on Dec. 19, 1946, with a history of two months' duration of malaise, chills, fever, and right anterior chest pain associated with cough, and a twelve pound weight loss. The referring doctor made a diagnosis of virus pneumonia. The patient had used oral mineral oil on retiring three times a week for many years. She had suffered from cardiospasm for thirteen years. Physical examination revealed a poorly-nourished, chronically ill-appearing, white woman without clubbing of the fingers. Her temperature on entry was 39.4° C. Dullness to percussion and decreased breath sounds were noted over the region of the right upper lobe posteriorly. Bronchoscopy revealed nothing other than reddening and swelling of the mucous membrane of the right upper lobe orifice. Esophagoscopy revealed spasm of the cardia and no other abnormalities. A clinical diagnosis of carcinoma or virus pneumonia was made. X-ray examination of the chest revealed two somewhat spherical areas of increased density, one in the subapical segment of the right upper lobe and one in the apical segment of the right lower lobe. At thoracotomy a firm mass in the subapical segment of the right upper lobe and another smaller lesion in the superior division of the right lower lobe were encountered. The cut surface of the lesion was yellowish-gray in color. There was destruction of the architecture. Yellowish conglomerate areas, 3 to 4 mm. in diameter, containing oil cysts were present. In some areas the pleura had thickened to 3 to 4 mm. Microscopic examination of the lesion revealed a typical paraffinoma in which the lipid stained with scarlet red and did not stain with osmic acid.

CASE 2 (E. L.).—This 46-year-old white man entered Barnes Hospital on May 4, 1947, with the chief complaint of chest pain on the left and fatigability for three years. An x-ray examination before admission had revealed a left lower lobe shadow. Bronchograms performed two weeks before the patient's hospitalization revealed some bronchiectasis in the left lower lobe. The patient gave a history of a tracheal intubation at the age of 6 years and

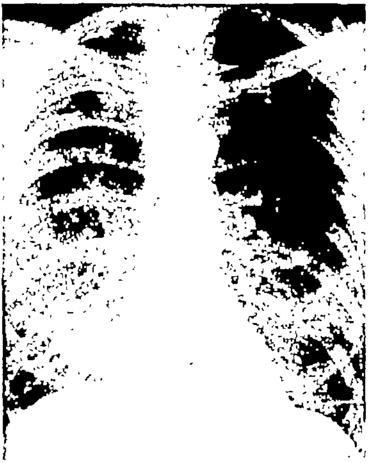

Fig. 1.—Roentgenogram of C. M., Case 3, showing obvious cystic changes in the upper lobes and the paraffinoma in the right lower lobe with relatively sharp periphery and feathering of the hilar aspect of the density.

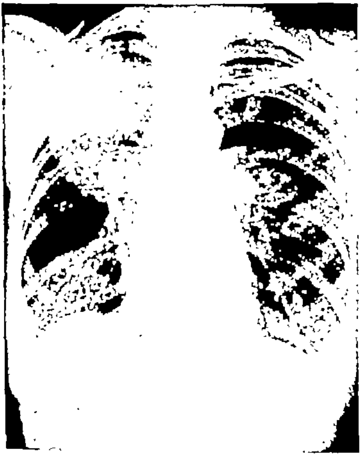

Fig. 2.

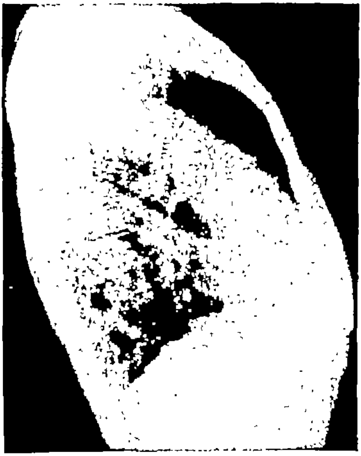

Fig. 3.

Figs. 2 and 3.—Posteroanterior and right lateral roentgenograms of B. A., Case 1, demonstrate lesions in two aspiration sites: the subapical segment of the right upper lobe and the apical segment of the right lower lobe.

hoarseness which had persisted from that time. He had suffered from chronic sinusitis and had been treated by an oily nasal spray and nose drops for an undetermined length of time. There was no history of hemoptysis. Physical examination revealed a thin white man without findings referrable to the chest and no clubbing of the fingers. Bronchoscopy was negative. At left thoracotomy a 4 by 3 cm. mass was present in the posterior basal segment of the left lower lobe. The overlying pleura was thickened and at the base and over the lateral pleura, tumorlike 3 to 5 mm. in diameter yellowish lesions were seen. On cut surface, a yellowish gray-black mottled surface was encountered which oozed a colorless oil. Microscopic examination of the lesion revealed a typical paraffinoma which stained with Sudan III and did not stain with osmic acid.

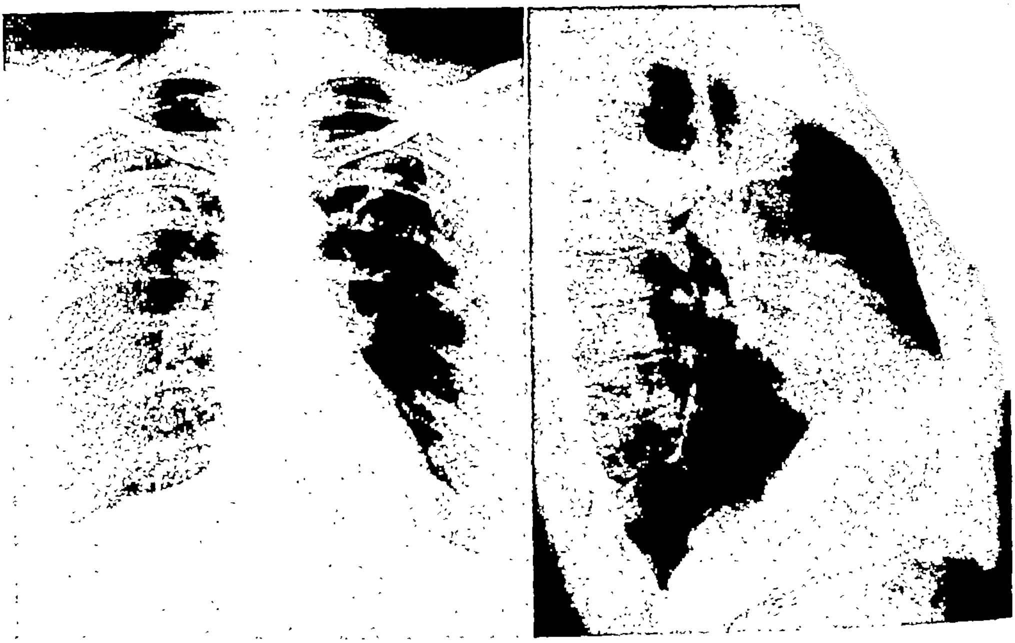

Fig. 4. Fig. 5.

Figs. 4 and 5.—Posterior-anterior and right lateral roentgenogram of R. B., Case 4, which illustrate the peripherally well-circumscribed lesion in the subapical segment of the right upper lobe.

Case 3 (C. M.).—This 51-year-old white man entered Barnes Hospital on Aug. 13, 1947, complaining of dyspnea of one year's duration, productive cough of six months' duration, and frequent lower respiratory infections for many years. He had had no hemoptyses. A bronchogram done two weeks before entry by the referring doctor was essentially noncontributory. The patient had used mineral oil at night for a laxative for as long as he could remember. Physical examination revealed a well-developed white man with an area of decreased resonance to percussion posteriorly over the right lower lobe region. There was no clubbing of the fingers. Roentgenologic findings consisted of bilateral emphysematous bullae in the upper lobes and a large radiopaque area in the right lower lobe which was thought to be a carcinoma. Bronchoscopic findings consisted of diffuse infiltration in the right main-stem bronchus with large amounts of thick, tenacious sputum being produced on that side. At operation the lesion was thought to be a carcinoma and a right pneumonectomy was performed. There were huge cysts in the right upper lobe and the posterior basal segment of the right lower lobe was occupied by a firm, 5½ by 4 by 4 cm. mass, peribronchial in location, with ill-defined margins and a yellowish-gray mottled oily cut surface. Microscopic examination revealed a typical paraffinoma which stained with Sudan III and not with osmic acid. The regional lymph nodes contained macrophages filled with mineral oil.

CASE 4 (R. B.).—This 52-year-old white woman entered Barnes Hospital in July, 1948, because a shadow was found in the right lung field on routine fluoroscopy. The patient had suffered from cardiospasm for ten years. She had used mineral oil at night for constipation for three to four years and had used Vick's VapoRub in the nostrils for colds and chronic sinusitis. She had no pulmonary symptoms and had had no hemoptysis. Physical examination revealed a well-developed, moderately obese white woman. Examination of the chest was negative. There was no clubbing of the fingers. X-ray examination revealed a circumscribed area of increased density in the right upper lobe in the subapical segment. Bronchoscopy was nonrevealing. A clinical diagnosis of lipoid pneumonia was made with the presence of carcinoma being strongly considered. At right thoracotomy the lesion was found to be a 5 cm. spherical mass in the subapical segment of the right upper lobe. Frozen section was done and was said to reveal carcinoma. A right pneumonectomy was performed. Satellite nodules were seen in the lower lobe. On cut surface the lesion was seen to be yellowish-gray, mottled, and exhibited sharp areas of transition between normal and involved parenchyma. There were small cystic spaces full of oil. Microscopic examination of the lesion revealed a typical paraffinoma with failure of the lipid to stain with osmic acid.

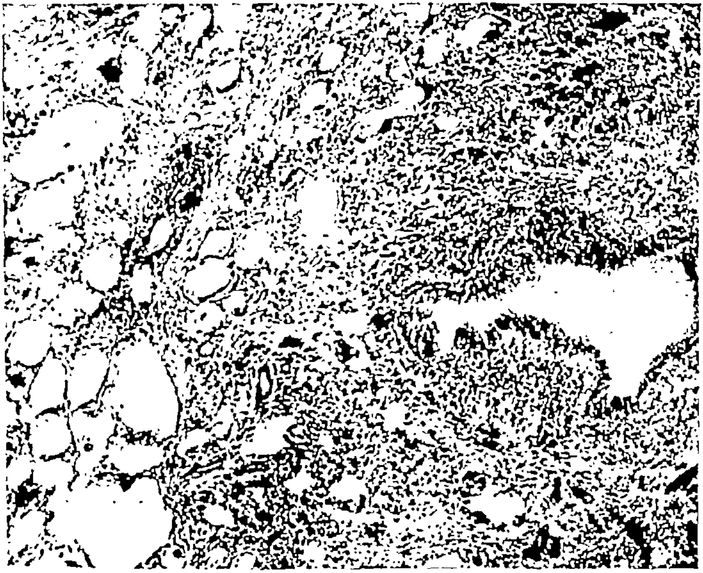

Fig. 6.—This photomicrograph of a hematoxylin and eosin section of the paraffinoma in Case 4, well demonstrates the variable sized spaces which contained oil.

CASE 5 (E. H.).—This 62-year-old white man entered Barnes Hospital in October, 1948. He was asymptomatic and gave a history of a lung lesion being found on a chance x-ray examination by a mobile unit. Bronchograms had been made by the referring physician and revealed an obstruction to the right middle lobe. He gave a history of using oily nose drops for chronic sinusitis for a period of about three years which ended five years before entry. He was a well-developed, well-nourished, white man with an anterolateral wedge-shaped area of dullness and decreased breath sounds over the right hemithorax. There was no clubbing of the fingers. A clinical diagnosis of carcinoma of the lung was made although repeated sputa were negative for tumor cells. Roentgenologic findings are shown in the accompanying photographs. On bronchoscopy the only abnormality in the tracheobronchial tree was posterior displacement of the orifice of the right lower lobe bronchus so that the

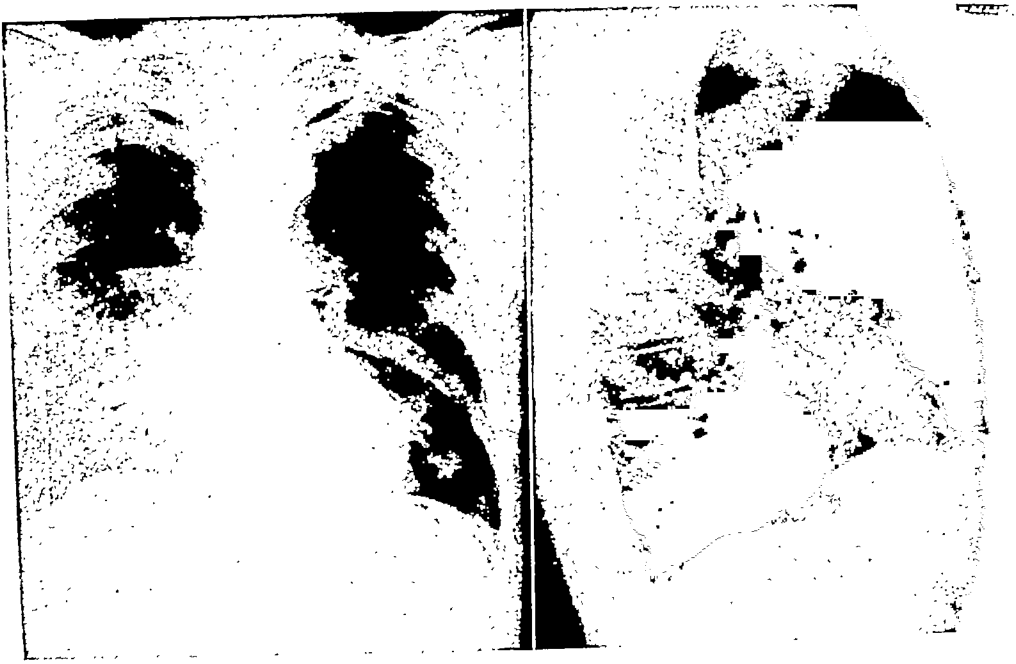

Fig. 7.

Fig. 8.

Figs. 7 and 8.—Posterior-anterior and right lateral roentgenogram of E. H., Case 5, showing middle and right lower lobe shadows which led to a thoracotomy.

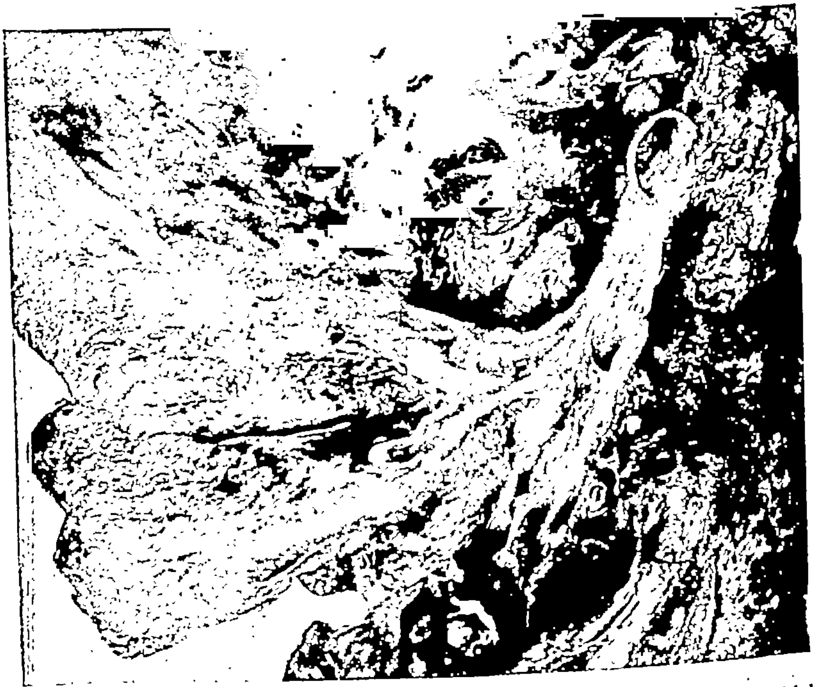

Fig. 9.—This photograph exhibits a cross section of the middle lobe lesion in which the gross resemblance to carcinoma is marked.

right middle lobe orifice was in line with the right main-stem bronchus. A right thoracotomy was performed and a yellowish-gray firm mass involving the parenchyma of the superior portion of the middle lobe causing extensive puckering of the pleura was found. This was associated with yellow-gray implants over the visceral and parietal pleurae and the pericardium. The lesion was thought to be a carcinoma with metastases to the pericardium and both pleural surfaces. A frozen section of the lesion was obtained and interpreted as showing carcinoma. A palliative resection was decided upon and carried out. Sections of the lesion described revealed a fibrotic lesion with complete erasure of the normal pulmonary architecture in which microscopic oil-filled spaces separated by fibrous tissue were seen. In some areas macrophages containing oil droplets could be seen. There were focal collections of lymphocytes. The regional lymph nodes contained macrophages with oil globules in their cytoplasm. The pulmonary lesion was a typical paraffinoma. The lipid material in the oil-filled spaces stained with Sudan III and failed to stain with osmic acid.

CASE 6 (R. O.).—This 52-year-old white man entered Barnes Hospital on April 7, 1949, because his physician discovered a lesion in the left lower lobe during a routine fluoroscopy. The patient had suffered for years from chronic sinusitis and constipation and had used mineral oil preparations for both lesions. He denied all pulmonary symptoms. He had never suffered an hemoptysis. Physical examination revealed a fairly well-developed white man who exhibited no physical findings of note on examining the chest. There was no clubbing of the fingers. Bronchoscopy was not performed. A clinical diagnosis of possible carcinoma in the left lower lobe was made preoperatively. At left thoracotomy the lesion was thought to be a paraffinoma on the basis of gross findings of a 5 by 5 cm. hard, mottled, yellow lesion in the anterior basal portion of the left lower lobe. Cut surface revealed miliary oil-filled spaces. Microscopic section of the lesion revealed a typical paraffinoma.

SUMMARY

1. Pulmonary paraffinoma is not uncommonly encountered by the thoracic surgeon. The lesion is clinically, radiographically, at operation, and even at frozen section confused with carcinoma, either primary or metastatic. Many lobes have been needlessly sacrificed by failure to recognize the true nature of this lesion.

2. Clinically the patient is usually an adult who may have no symptoms or symptoms mimicking bronchiogenic carcinoma, even hemoptysis. The patient almost always gives a history of use of mineral oil or one of its medicated preparations either orally, nasally, or even intratracheally. There may or may not be an associated neurologic lesion resulting in impairment of ability to swallow or mechanical interference with deglutition as with diverticula and cardiospasm.

3. Roentgenologically, circumscribed tumorlike shadows in aspiration areas without hilar adenopathy and with peribronchial infiltration, especially in the lower lobes, are present. The lesion is roentgenologically more striking than the patient's clinical symptoms would lead one to expect. The lesions are often multiple and frequently bilateral.

4. At operation the lesion may so mimic carcinoma as to result in needless pneumonectomy when lobectomy would have sufficed.

5. Pulmonary paraffinoma is often misdiagnosed and it is hoped that renewed attention to the subject will stimulate more accurate diagnoses. There has been some evidence suggesting that mineral oils are carcinogenic.

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DISCUSSION

DR. J. E. DAILEY, Houston.—We have had three cases of lipoid pneumonia upon which we have operated, two of which closely resembled the appearance so well described by Dr. Berg. I would like to show one case that was rather different, which began as an acute inflammatory type of lesion. This was a man about 38 years old who had been in the habit of using oily nose drops for several months.

(Slides.) This started with an acute onset of fever, 101° to 102° F., and the x-ray appearance of pneumonia, which apparently did not resolve. The first slide, in March, 1949, is shown on the left; on the right, one week later, showing a marked change in the appearance of the lesion which at first looked like an inflammatory type lesion. He improved somewhat and his temperature decreased. However, he began to expectorate some bloody sputum. (Slide.) This shows, two months after the first roentgenograms were taken, an atelectatic type of lesion. This was the time at which we first saw the patient and, of course, without the first two roentgenograms our first impression would be carcinoma of the lung. When we obtained the first roentgenograms there was a little doubt because of the inflammatory appearance. Bronchoscopic studies were performed, Papanicolaou slides and *Gelfoam* sponge preparations were made. All were negative for any evidence of malignant cells.

We operated on him and the following is a postoperative roentgenogram. At operation the lesion still appeared to be an inflammatory lesion, rather than tumor, so we elected to do only an upper right lobectomy. The next slide shows the granulomatous type of lesion that was present in the apical division. The next slide shows the microscopic specimen, illustrating well the lipoid content of the cells.

DR. JOHN J. HARTER, Louisville, Ky.—The industrial occurrence of paraffinoma of the lung has been mentioned before in the literature. I simply want to bring it to your attention again. We have had two patients in whom the history was very definite; one was a Diesel motor mechanic who inhaled Diesel fuel oil. The other was a gear-cutter operator. Gear-cutter machines, I am told, use oil under very high pressure; the lines occasionally break and he would inhale the oil. I think it is well to remember that the increasing use of oil under high pressure may well give us more of these paraffinomas in the future. Both our patients were operated upon for lung abscess and lobectomies were done. The paraffinoma was found to be the cause of the lung abscess in each case.

DR. JOHN R. MCDONALD, Rochester, Minn.—I wish to point out that not all oil granulomas of the lung are due to mineral oil. I want to mention three cases which illustrate the various types of oil granuloma of the lung which are of importance to the surgeon.

The first case is that of a young man, 17 years of age, who had a history of chills and fever of four months' duration. A roentgenogram of his thorax disclosed a shadow in the left lower pulmonary field. A left lower lobectomy was done. An aberrant vessel to this left lower lobe was found coming from the aorta. After careful dissection of the bronchial tree of the lower lobe, it was determined that there was no communication between this bronchus and the rest of the bronchial tree. The lobe itself was airless, consolidated, and yellow. The diagnosis was pulmonary sequestration with lipoid pneumonitis of the lobe. Microscopically the pulmonary alveoli and bronchi were filled with inflammatory cells and a great deal of lipid was present in phagocytes. Gross chemical studies of this tissue revealed a total lipoid content of 4.1 per cent made up of cholesterol esters, lecithin, and fatty acids. In this case it is obvious that the oil is the result of a breakdown of the cells in the lobe by which process invisible lipids become visible.

The second case is that of a young woman who had bronchiectasis. In order to determine the extent of the bronchiectasis, a bronchogram had been made with the use of Iodochloral. The oil base for Iodochloral is peanut oil. At the time of lobectomy, two weeks after the bronchogram had been made, consolidated pinkish-yellow areas were found in the resected lobe which microscopically demonstrated an oil granuloma. Gross chemical studies were done on the consolidated granulomatous areas and the nonconsolidated areas of the same lobe. These demonstrated a large amount of iodine in the consolidated granulomatous areas and practically none in the nonconsolidated areas. Such evidence is proof that this granuloma was due to the Iodochloral.

The third case is that of a patient having a mineral oil granuloma. Thoracotomy had been done to determine the nature of a roentgenographic shadow in the lung. At the operating table a piece of tissue was removed from the mass for microscopic diagnosis and a tentative diagnosis of mineral oil granuloma was made from the fresh frozen section. Lobectomy was then done. The oil was extracted from the lesion with fat solvents. It proved nonreactive to acids and alkalies. It was, therefore, concluded that this oil belonged to the petroleum group of lipids. After operation, a history of repeated instillations of mineral oil was obtained in regard to this patient.

I consider it much more accurate to determine the type of oil present in these various granulomas by means of gross chemical studies than by the use of histologic preparations utilizing the various fat stains.

DR. A. J. GRACE, London, Ontario.—I want to emphasize what was brought out by Dr. Berg and Dr. Burford—that this is a problem which we can diagnose wrongly unless alive to its existence and frequency. I made a mistake, too, and want to present briefly slides which illustrate one such case where pneumonectomy was done. I think the principle must be stressed, during these days when we are urging general surveys of chest cases and correct treatment for any circumscribed or other mass that is found, that we must not overtreat these cases nor do unnecessary major operations, and this case is certainly an unfortunate illustration of that point.

(Slides.) This is a man nearly 60 years of age, who had minimal symptoms. You will note at the right base a collapsed middle lobe. The picture does not show well a circumscribed mass which was picked up in the course of x-ray studies. The next slides show the specimen removed by pneumonectomy. The process involved the lower as well as the middle lobe, and that was the reason for the pneumonectomy.

The principle to be emphasized is that which Dr. Berg brought out, that we must be on the lookout for this lesion. It is a relatively common one. Mineral oil is being used too much by the public, it has some dangers, and I think we should make that fact known. This case illustrates the point that the symptoms, although marked, were not in keeping with the suspected diagnosis of carcinoma, and I think we should have considered that. We have seen one similar case since in which operation was avoided.

DR. BURFORD (closing).—Dr. Berg has indicated the reason for our interest in this lesion. Failure to recognize the probability of a paraffinoma by neglecting to elicit the pertinent historical facts, and lack of proper conception of the radiographic appearance, will often lead to the development of a cycle of vicious events which may even encompass the surgical pathologist. The result is the needless sacrifice of normal lung. Recognition of the principles stressed by Dr. Berg has enabled us to diagnose this disease with fair accuracy, and leads us to believe that far fewer mistakes will be made in the future.

Dr. Grace has shown a beautiful example of a true paraffinoma. I would like to thank him for his remarks and particularly for his choice of a case.

Dr. McDonald's case was not what we are talking about today. We purposely and carefully excluded this type of lesion from our group in order that clarity of thinking may be attained in relation to the true paraffinoma.

We disagree vehemently that one needs more than the hematoxylin and eosin and osmic acid stains to diagnose histologically the true paraffinoma.

SURGICAL TREATMENT IN PULMONARY COCCIDIOIDOMYCOSIS

Preliminary Report of Thirty Cases

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SURGICAL management of thirty cases of pulmonary coccidioidomycosis is reviewed. Operative criteria are established. The results obtained in this limited number of selected cases are extremely encouraging and appear to warrant further analysis.

The complications of pulmonary coccidioidomycosis are: (1) fibrosis of varying degrees of parenchymal infiltration; (2) coccidioma (this term has been employed by the authors to represent the circumscribed density occurring in the lung parenchyma, as a coccidioidal granuloma, comparable to a tuberculoma and indistinguishable both roentgenologically and anatomically); (3) dissemination; (4) pleural effusion; (5) bronchiectasis (extensive study of bronchoscopy and bronchography findings has yielded considerable information which tends to prove that bronchiectasis is a common sequela of pulmonary coccidioidomycosis); and (6) cavitation.

Of these six complications, cavitation presents the greatest dilemma to the attending physician as to both prognosis and treatment. The course of cavities may be divided into an acute and a chronic phase. The acute cavity appears with the parenchymal infiltration and disappears completely with the resolution of the infiltration. The typical chronic cavity persists apparently with a minimal or no zone of fibrosis around it. The minimum period between these two phases is usually from six to eight weeks. Another interesting finding is the lack of correlation between the extent of parenchymal involvement during the acute phase and the development of complications.

The complications occurring in the medically treated or untreated cavities are:

1. Giant cavity
2. Secondarily infected cavities
3. Rupture of cavity
    a. spontaneous pneumothorax
    b. empyema
    c. bronchopleural fistula
4. Nonexpansile lung
5. Hemoptysis
    a. continued
    b. severe

AUTHORS' SERIES

Significant data pertaining to the thirty patients included in this series are summarized in Table I. Diagnosis was confirmed in all instances by one or

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Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 16-18, 1950.

TABLE 1

CASE NUMBER	AGE (YR.)	SEX	RACE	DURATION OF ILLNESS	MEDICAL TREATMENT EMPLOYED	DIAGNOSIS CONFIRMED BY	OPERATIVE INDICATIONS	OPERATIVE PROCEDURE	COMPLICATIONS	PRESENT CONDITION
1. C. S.	36	M	W	8 yr.	Rest cure; diagnosed tbc until 1945	Spherules in sputum; pos. blood	Giant cavity, secondarily infected	Left upper lobectomy	None	Symptom free; ret. to work 3rd P.O. wk.
2. J. L.	48	M	W	Unknown	Rest cure; rt. phrenic; penicillin IM and aero.	Spherules in sputum; pos. blood; high blood titer, bordering on dissemination	Giant cavity, secondarily infected	Right pneumonectomy	Cocc. empyema controlled by thoracoplasty	Symptom free; ret. to work 4th P.O. mo.
3. L. L.	49	M	Mexican	4 yr., 8 mo.	Rest cure; penicillin IM and aero., diagnosed as lung abscess	History pos. skin test; neg. tbc; typical thin-walled cavity	Giant cavity, secondarily infected	Right pneumonectomy	Died of coronary thrombosis 4th P.O. day	
4. F. D.	47	M	W	8 mo.	Rest cure	Spherules; pos. blood	Giant cavity, secondarily infected	Right pneumonectomy	None	Symptom free; ret. to work 2nd P.O. mo.
5. F. T.	29	M	W	9 yr.	Rest cure; bilat. phrenic; bilat. pneumothorax; pneumoperitoneum	Spherules; pos. blood; pos. tbc sputum	Giant cavity	Right pneumonectomy	None	Symptom free; released from San. 8 mo. P.O.
6. J. P.	23	M	W	6 yr.	Pleural effusion, aspiration; bed rest	Pos. skin; neg. tbc; typical history and x-ray	Hemoptysis; large cavity	Right lower lobectomy	None	Symptom free; ret. to work
7. J. T.	19	M	W	5 mo.	Partial bed rest	Spherules from pleural fluid; culture pos.; pos. serology, range of dissemination	Empyema	Left lung decortication with removal of cyst	None	Symptom free; ret. to work 3rd P.O. wk.
8. G. R.	43	M	W	3 yr.	Bed rest, intermittent	Spherules in pleural fluid; pos. blood and pos. skin	Empyema	Decortication, left lung	None	Symptom free; ret. to work 2nd P.O. mo.

9. G. J.	35	F	W	21 mo.	Intermittent bed rest	Spherules in sputum; *pos.* skin, neg. tbc; G.P. pos. for tbc	Hemoptysis; *gen. malaise*	Segmental *lobectomy,* left upper	None	Symptom free; ret. to work 2nd P.O. mo.
10. W. J.	33	F	W	9 mo.	Bed rest, intermittent	Pos. skin; pos. blood	Hemoptysis; gen. malaise	Segmental rt. upper lobe	None	Symptom free; ret. to work 3rd P.O. wk.
11. L. C.	30	F	W	9 mo.	Bed rest; rt. pneumothorax, pneumoperitoneum	Pos. skin; pos. blood; pos. sputum culture	Blocked ballooning cavity	Right lower lobectomy	None	Symptom free; ret. to work 3rd P.O. wk.
12. W. D.	34	M	W	2 yr.	None	Culture pos.; path. specimen, spherules	Differential of carcinoma and coccidioma	Segmental left lower lobe	None	Symptom free; ret. to work 4th P.O. wk.
13. J. M.	31	M	W	4 yr.	Bed rest 16 mo.; rt. pneumothorax; pneu*moperitoneum;* rt. phrenic, temporary	Pos. skin; pos. blood; pos. sputum; sputum *pos. tbc*	Failure of medical Rx; hemoptysis	Right lower lobectomy	Pleural effusion lt. tbc contra-lat. lung; actinomycosis, rt. lower lobe	Symptom free; ret. to work 3rd P.O. mo.
14. F. S.	16	M	W	12 mo.	Bed rest; phrenic crush; pneumothorax; pneumoperitoneum	Pos. skin; pos. blood; pos. sputum	Secondarily infected cavity	Segmental lobectomy	None	Symptom free; ret. to work 4th P.O. wk.
15. M. L.	36	M	W	6 mo.	Bed rest	Culture positive	Empyema, left pleural space	Decortication, empyema space	None	Symptom free; ret. to work 6th P.O. wk.
16. C. B.	47	M	W	2 yr.	Bed rest	Skin test pos.; comp. fix. neg.; typical history and thin-walled cavity	Cavitation, secondarily infected	Pneumonectomy	Associated primary ca. of the lung	Symptom free; ret. to work 2nd P.O. mo.
17. B. S.	17	F	W	20 mo.	Bed rest	Pos. skin; neg. tbc; typical history and typical thin-walled cavity	Hemoptysis, secondarily *infected*	Rt. upper lobectomy	None	Symptom free; ret. to work *3rd* P.O. wk.

(Continued on following pages.)

TABLE I—CONT'D

CASE NUMBER	AGE (YR.)	SEX	RACE	DURATION OF ILLNESS	MEDICAL TREATMENT EMPLOYED	DIAGNOSIS CONFIRMED BY	OPERATIVE INDICATIONS	OPERATIVE PROCEDURE	COMPLICATIONS	PRESENT CONDITION
18. R. L.	36	F	W	4 mo.	Bed rest; penicillin	Pos. skin test; pos. culture from specimen	Blocked secondarily infected cavity	Right lower lobectomy	None	Symptom free; ret. to work 2nd P.O. mo.
19. M. S.	40	F	W	22 mo.	Penicillin; bed rest	Pos. skin test; pos. blood	Hemoptysis, giant cavity, secondarily infected	Right lower lobectomy	None	Symptom free; ret. to work in 6 wk.
20. M. C.	38	M	W	Unknown	None	Spherules; pos. skin test; neg. tbc	Expanding density, rt. lower lung	Segmental resection	Prolonged pocket of fluid	Symptom free; ret. to work 3rd P.O. mo.
21. C. A.	39	M	W	Unknown	None	Spherules from specimen; pos. skin; neg. tbc	Rounded density rt. upper lobe; diff. bronchiogenic ca.	Segmental resection	None	Symptom free; ret. to work 3rd P.O. wk.
22. M. K.	36	F	W	16 mo.	Pneumothorax; bed rest	Pos. skin test; pos. comp. fix.	Continued hemoptysis	Left upper segmental lobectomy	None	Symptom free; ret. to work on 2nd P.O. wk.
23. R. S.	34	M	W	12 yr.	Bed rest; drainage of empyema, 2-9-40	Spherules in pleural fluid	Ruptured cavity mixed empyema; bronchopleural fistula; nonexpansile lung	Decortication supplementary thoracoplasty	None	Symptom free; ret. to work 4th wk. P.O.
24. E. J.	30	M	C	22 mo.	Bed rest; antibiotics	Pos. skin test; pos. blood; spherules in sputum	Hemoptysis, secondarily infected cavity	Left upper lobectomy	P.O. atelectasis controlled by bronchoscopy and aspiration	Symptom free; delayed P.O. re-expansion

25. V. R.	42	F	W	7 yr.	Antibiotics and sulfonamides	Pos. skin test; tbc neg.; typical thin-walled cavity	Bronchiectasis, secondarily infected	Rt. upper and middle lobectomy	None	Symptom free; ret. to work in 4 wk.
26. M. S.	26	M	C	9 mo.	Bed rest	Microscopic section of surgical specimen; comp. fix. neg.	Cavitation with severe and continued hemoptysis	Lt. upper lobectomy	None	Returned to work in 3 wk.
27. D. B.	41	M	W	Pleural effusion	Bed rest, thoracentesis	Neg. skin test; spherules recovered on culture; comp. fix. neg.	Cavity and unexpanded lung	Decortication, segmental resection of cavity	None	Returned to work in 8 wk.
28. L. H.	19	M	W	4 mo.	Bed rest, thoracentesis	Spherules found in spec. by microscopic examination; pos. skin test; tbc neg.; comp. fix. neg.	Pleural effusion; unexpanded lung; broncho-pleural fistula	Segmental lobectomy, dorsal div., lt. lower lobe and complete decortication	None	Complete re-expansion, returned to school
29. L. U.	45	F	W	1 yr.	Bed rest; pneumothorax; pneumonolysis	Pos. skin test; pos. tbc; acid-fast in sputum; confirmed by microscopic section, *Coccidioides immitus;* serology equivocal	Failure of collapse therapy	Rt. upper lobectomy		Returned to the sanatorium for further observation
30. L. C.	25	M	W	3 yr., 3 mo.	Observation for rounded density	Pathological section and culture; comp. fix. neg.; skin test pos.	Expanding lesion; cavity from shelling out of coccidioma	Rt. lower lobectomy	None	Returned to work in 4 wk.

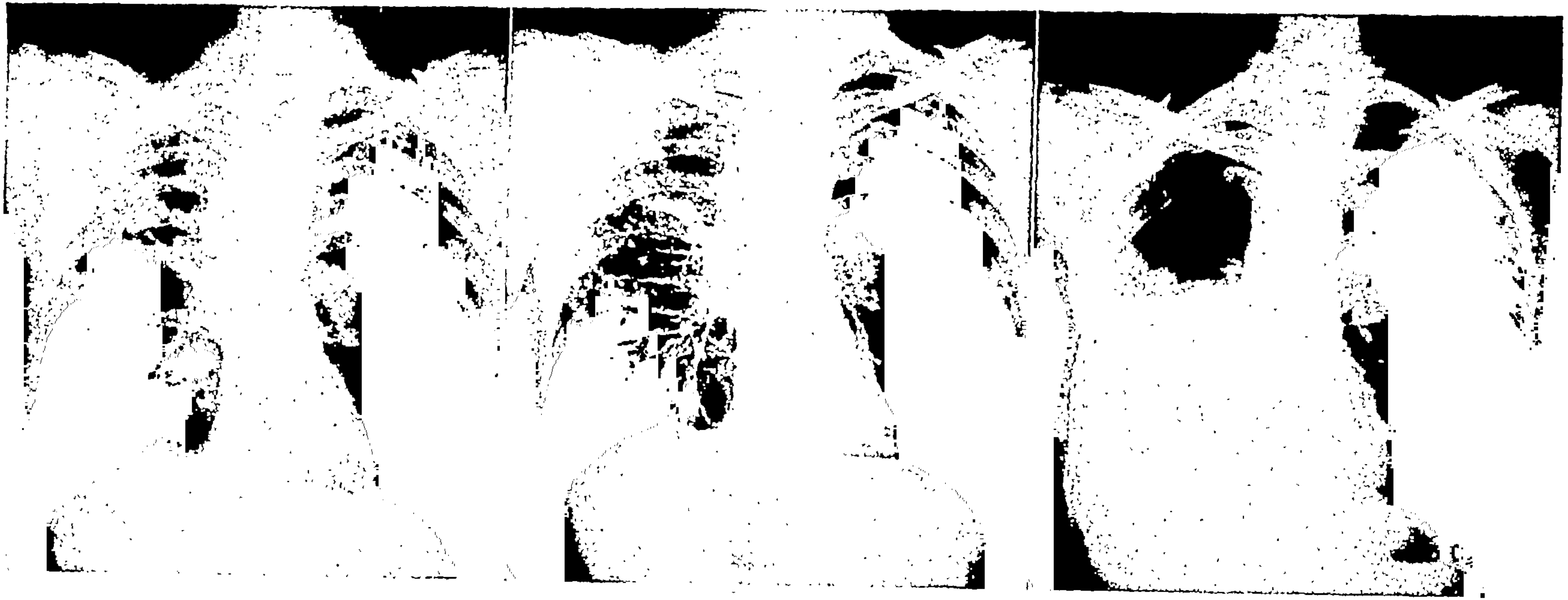
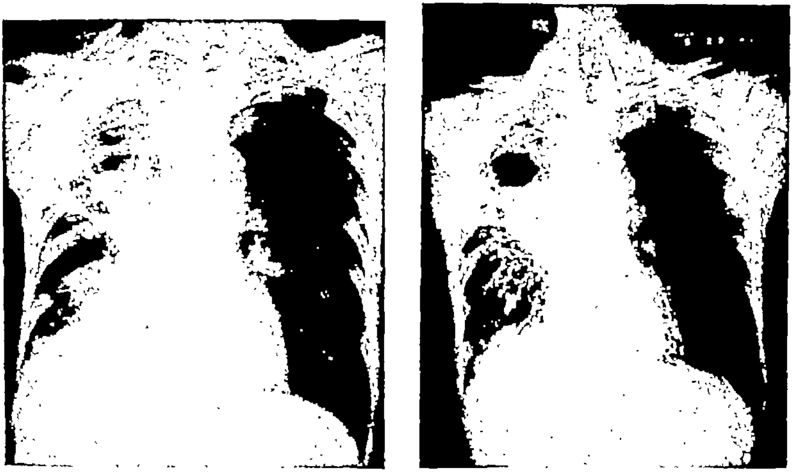
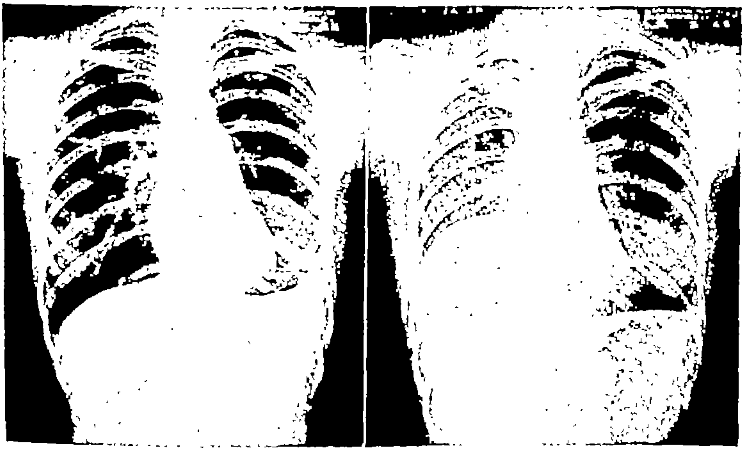


Fig. 1 (Case 2).—*A*, Giant cavity; *B*, bronchiectasis, lower right lung field; *C*, postoperative.



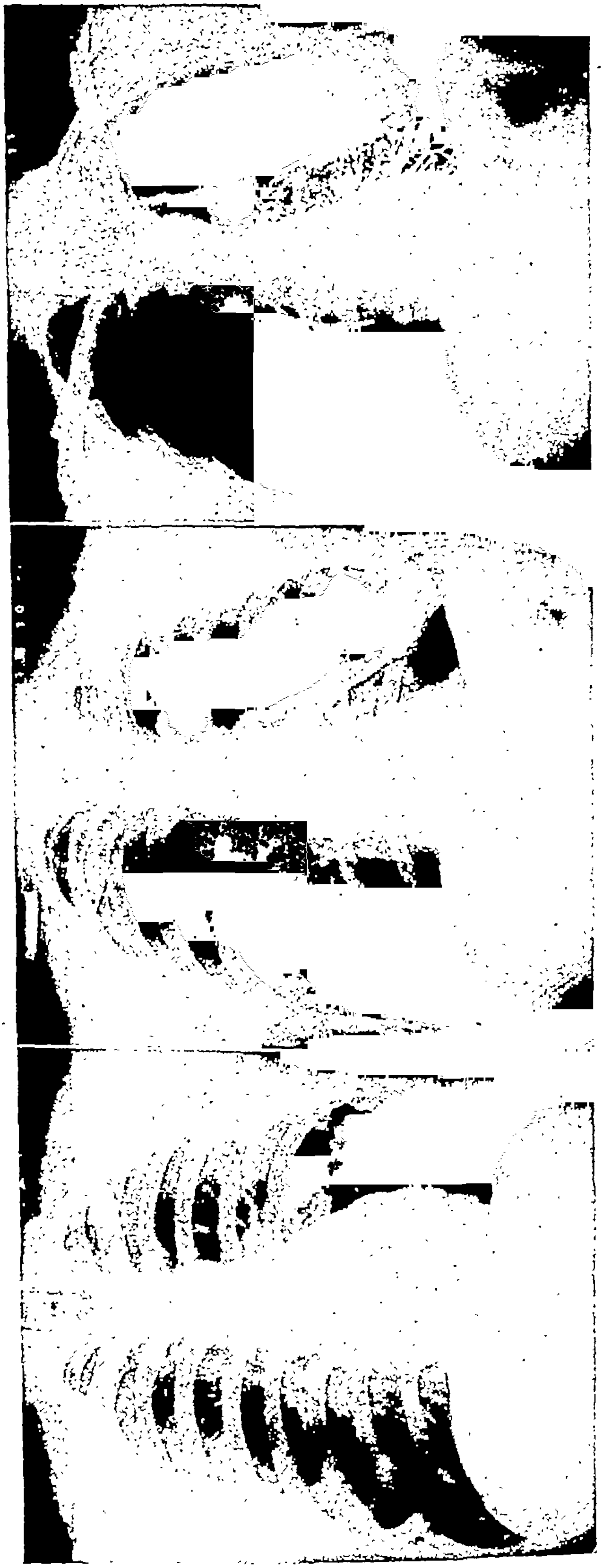
A. *B.*

Fig. 2 (Case 3).—*A*, Secondarily infected cavity with pyogenic organisms; *B*, bronchiectasis of right middle and lower lobes.



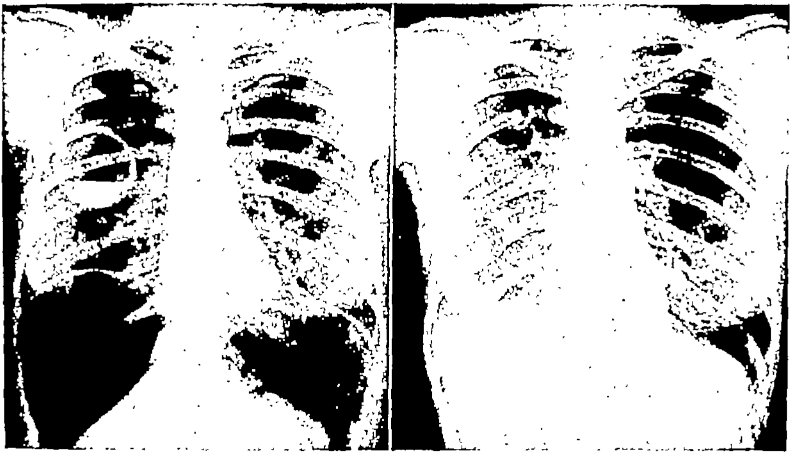
A. *B.*

Fig. 3 (Case 5).—*A*, Coccidioidomycosis cavity, left hilar area; *B*, coccidioidomycosis cavity secondarily infected with pulmonary tuberculosis.



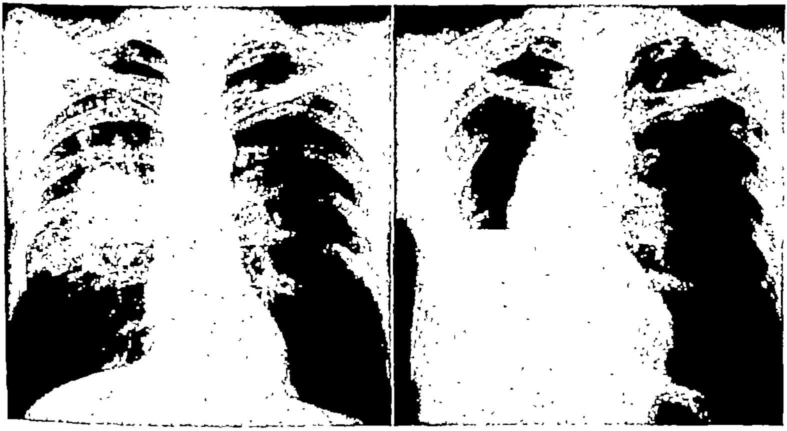
A. B. C.

Fig. 4 (Case 8).—*A*, Cavity, under medical management, ruptured causing spontaneous pneumothorax with temporary bronchopleural fistula; *B*, coccidioidomycosis empyema with nonexpansile lung; *C*, preoperative, normal bronchial tree.



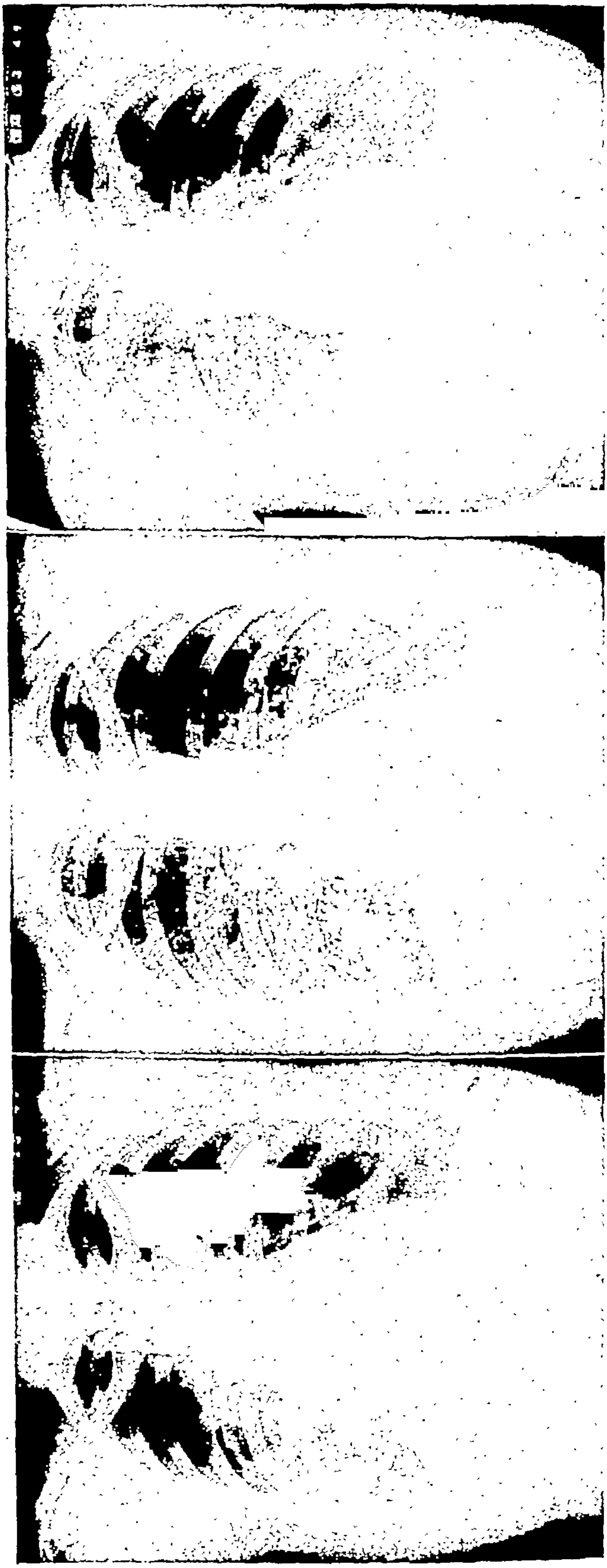
A. B.

Fig. 5 (Case 11).—A, Blocked cavity; B, postoperative.



A. B.

Fig. 6 (Case 16).—A, Cavitation, secondarily infected, associated primary carcinoma of the lung; B, postoperative.



A. B. C.

Fig. 7 (Case 10).—*A*, Large cavity, right lower lobe; *B*, bronchogram; *C*, postoperative.

more of the following conclusive laboratory methods: spherules in sputum; complement-fixation test; culture; guinea pig inoculation; and/or pathologic specimen. Five cases used in this series were included when they met the following criteria: typical history of acute pulmonary coccidioidomycosis, thin-walled cavity by roentgen examination, negative Mantoux and positive coccidioidin skin tests.

It is interesting to note that the diagnosis of coccidioidomycosis is occasionally easier to make in vivo than on examination of the pathologic specimen. The coccidioidal cavity, which in the acute phase allows recovery of the *spherules from the sputum, may lose its identity in the presence of a super*imposed infection of either tubercle bacilli or pyogenic organisms.

Types *of operations employed in the series were:*

1. Pneumonectomy	5
2. Lobectomy	11
3. Segmental lobectomy	8
4. Wedge resection with decortication	5
5. Decortication plus thoracoplasty	1
Total	30

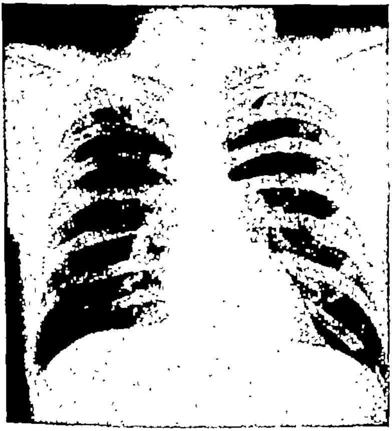


Fig. 8.

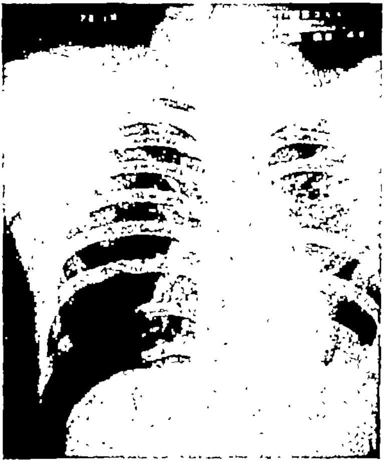


Fig. 9.

Fig. 8 (Case 21).—Coccidioma.
Fig. 9 (Case 7).—Postoperative film following decortication.

Twenty-seven of the thirty patients underwent operations for cavities, only six patients received operations for empyema, five of which had cavity resections, and three operations were performed in order to rule out the presence of carcinoma. Case 16 had associated primary carcinoma of the lung. In Case

11, the rapid destruction of lung parenchyma under medical management made the operation an emergency. In Case 7, concern over surgical intervention was expressed by the medical department because the blood titer was in the dissemination range. Despite this fact, as well as the fact that a cavity was removed and a decortication performed in the presence of a coccidioidal empyema, no clinical dissemination occurred postoperatively and the titer fell. In Cases 2, 3, 5, and 13, resection was done under local anesthesia in order to avoid postoperative complications arising from drainage. Cases 5, 9, 13, and 29 were complicated by tuberculosis in addition to coccidioidomycosis. In Cases 2 and 3, voluminous sputum due to secondarily infected cavities was present. The only death in this series was due to a coronary occlusion several days following operation.

DISCUSSION

Statistically, pulmonary coccidioidomycosis may be considered a benign disease even in areas in which it is endemic. However, such statistics have little significance to the patient hemorrhaging from a coccidioidal cavity, to the patient with a secondarily infected cavity (lung abscess), to the patient with dyspnea from an unexpanded lung, or to the patient misplaced in a tuberculosis sanatorium. The inaccuracy of general statistics regarding pulmonary coccidioidomycosis is perhaps directly attributable to three factors:

1. No simple diagnostic test is readily available in areas in which the disease is endemic.

2. No clinical symptoms manifest themselves after the patient has left the endemic area with the result that the proper diagnosis frequently is overlooked.

3. The majority of extrapulmonary lesions warrant hospitalization and extensive laboratory procedures, thus overshadowing chronic pulmonary lesions which may be treated on an ambulatory basis.

There is little doubt that certain selected cases will respond to medical treatment. It has been unquestionably proved by Winn* that many cases of coccidioidal cavitation can be cured by collapse therapy. In our series of cases where medical treatment was employed, the results were unsatisfactory. The medical measures ranged from bed rest, phrenic nerve crush, pneumothorax and pneumoperitoneum to months of hospitalization in tuberculosis sanatoria. Postsurgical examination of the specimens revealed two causes for the failure of collapse therapy: (1) the cavity, although appearing thin-walled roentgenographically, actually was composed of a dense fibrinous wall which could be obliterated with difficulty by direct manual pressure; and (2) dense adhesions were present from the cavity wall to the thoracic cage. The rationale of surgical removal in such cases was clearly established. Although the records showed that operative procedures in instances of extrapulmonic infections of coccidioidomycosis usually had resulted in further spread of the disease process, the progressive deterioration of certain patients under medical management left pulmonary resection as the only means of arresting the disease.

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*W. A. Winn, Springville, Calif., personal communication.

The remarkable recovery without complications which followed the initial operations in this series, coupled with the fact that decortication was performed in the presence of an active coccidioidal empyema with complete re-expansion of the lung, the wound healing by primary intention—these results led us to conclude that suitability for operation could be determined without regard to *the etiological nature of the pathologic condition or whether the disease was in* a dormant or active phase. Consequently, we disregarded all laboratory findings and viewed the complication of pulmonary coccidioidomycosis from the mechanical standpoint only. A close analysis of the data in Table I further substantiates our conclusion that the medical status of the disease has little effect on either the indications for operation, the choice of operative procedure, or the postoperative results. Only in determining the priority for the patient on the operating room schedule is the medical status of the disease significant.

SUMMARY AND CONCLUSION

1. A series of thirty cases of pulmonary coccidioidomycosis treated by surgical methods is presented.

2. Surgical treatment in pulmonary coccidioidomycosis can be used to prevent death and is effective in arresting the disease process.

3. Surgical treatment in pulmonary coccidioidomycosis does not cause dissemination of the disease to the skeletal or nervous system, but may even prevent dissemination.

4. Surgical treatment is definitely indicated in pulmonary coccidioidomycosis in the following conditions:

   1. Specific types of cavities
      - a. Giant cavity
      - b. Secondarily infected cavity
      - c. Blocked cavity
   2. Rupture of cavity
      - a. spontaneous pneumothorax
      - b. empyema
   3. Nonexpansile lung
   4. Hemoptysis
      - a. continued
      - b. severe
   5. Coccidioma—expanding lesion
   6. Failure of medical treatment (collapse therapy, etc.)

5. Coccidioma, which is usually single but may be multiple, must be differentiated from a tuberculoma, hamartoma, and both primary and metastatic carcinomatous lesions.

6. Lung complications resulting from pulmonary coccidioidomycosis should be evaluated surgically from the standpoint of pathologic lesions without regard to the fungus origin or activity of the disease.

7. Surgical treatment in selected cases of pulmonary coccidioidomycosis results in rapid rehabilitation of the patient.

8. The combination of pulmonary cavities due to tuberculosis and coccidioidomycosis does not constitute a contraindication to surgical management.

DISCUSSION

DR. W. L. ROGERS, San Francisco.—I have followed Dr. Cotton's work with a great deal of interest and I am sure you will agree that after this excellent report, which I believe represents the largest surgical experience reported to date in dealing with the complications of pulmonary coccidioidomycosis, together with the excellent report by our Denver colleagues as a result of their experience at Fitzsimons some two years ago before this organization, we are able to crystallize very well indeed our thinking in dealing with these complications. In the résumé, I believe point number six covers it very well. Lung complications resulting from pulmonary coccidioidomycosis should be evaluated surgically primarily from the lesion in question and the symptoms thereof, without regard to the specific fungus origin or perhaps the activity of the disease. This statement appears to me to be of primary significance while the surgical approach or technique used in the individual case may be considered quite secondary.

In our small series we have used lobectomy, wedge excision, decortication on the visceral pleural surface and, in four instances which may be of interest and sufficiently significant to relate, we have done a simple enucleation of the residual cavity. In each of the four cases the presenting symptom was repeated hemoptysis, a symptom mentioned by Dr. Cotton in some cases with a residual cavity. The existing pathology in each instance was a thin-walled cavity superficially located. In two instances, because of an incomplete fissure between the apex of the lower lobe and the inferior posterior segment of the upper lobe, the cavity transcended into two lobes. Very simply these cavities could be enucleated, vessels and small bronchi being ligated as encountered, and the defect created left open. Bearing in mind the importance of rapid expansion, especially when dealing with specific infections, we have utilized low-grade suction postoperatively in all these cases without encountering any trouble with the pleura.

I think it also highly important that in no instance was there clinical manifestation of reactivity, x-ray manifestation of activity, or serologic manifestation of reactivity in any of these people so treated. This last statement also applies to our other cases treated perhaps in a more orthodox manner.

COL. JAMES H. FORSEE, Denver.—Two years ago we reported before this Association our experience at Fitzsimons Hospital in the management of 13 patients with pulmonary coccidioidomycosis with focalized lesions. In view of Dr. Cotton's splendid report it may be of interest to note the follow-up studies on the 13 cases.

Four patients had granulomatous lesions removed and all have remained well. Nine patients had lobectomies performed for cavitary lesions. One patient developed pulmonary tuberculosis. After a review of the surgical specimen removed there was no evidence of tuberculosis present in this lung. Two patients are salesmen (one on a half-day basis), four are doing active military duty, two have been for the past year and one-half actively engaged as truck drivers.

We have continued to recommend pulmonary resection in coccidioidomycotic cavities if there are symptoms. These symptoms, as mentioned, are generally hemoptysis and pain. Our results so far, we believe, have been reasonably satisfactory, but we are not at all sure that the complete answer has been given in the treatment of cavities by lobectomy or pulmonary resection. We believe, however, at the present time, that this is the best method of management of persistent cavitation.

DR. JOSEPH A. WEINBERG, Van Nuys, Calif.—There is one point that I feel should be brought out particularly in discussing surgical treatment of granulomatous or cystic coccidioidomycosis of the lung. One reason for feeling our way cautiously in applying surgery up to the present time is that we have known so little about why the disease sometimes manifests itself as a localized disease and at other times becomes a disseminating disease. Although not proved, it has been suspected that the trauma of surgery during the acute stage of high complement fixation titer might convert a localized lesion into a disseminating infection. This question assumes grave significance when it is considered that about one-half the disseminating cases are fatal. Therefore, it might be well, while we are feeling our way with surgery in the localized lesions, to limit ourselves to those cases with negative complement fixation and to those cases with low complement fixation in a phase of declining titer.

I would like to show one case of rather extensive surgery which probably would not have healed otherwise, at least not as quickly. (Slide.) In this case thoracoplasty was performed after drainage of an empyema which was secondary to a pulmonary lesion of the type Dr. Cotton has shown. This slide shows the persistent space after thoracoplasty; even further thoracoplasty failed to heal the empyema or the multiple fistulas associated with it. The next slide is after extrapleural pneumonectomy, that is, pneumonectomy with decortication. Following this procedure the empyema together with the multiple fistulas healed. Convalescence was uneventful and the patient remains well today.

I have three slides from this case which may be of interest from the standpoint of histopathology. In this slide we see a sporulating granule lying free in the pulmonary tissue, with its double refractile membrane. The next slide shows a characteristic granule with epithelioid cells, giant cells, and a few leucocytes in the specimen. Here we see two empty sporules, showing that they are nonviable. The next rather interesting high power slide shows this giant cell apparently extending out pseudopodia-like processes to engulf the two sporules.

DR. COTTON (closing).—The chronic coccidioidal cavity should be included in the differential diagnosis of all chronic cavities. Modern day transportation has transformed an endemic disease into a pandemic disease. Widespread medical interest in coccidioidomycosis is manifested by more than 200 articles in the literature, with cases reported from the New England States to Argentina, South America.

Dr. Rogers has summed up the treatment of the chronic coccidioidal cavity very completely. It may be considered from the mechanical standpoint alone, and the disease process itself can be disregarded when the patient needs definitive surgical treatment.

PECTUS EXCAVATUM

Case Report With Pre- and Postoperative Angiocardiographic Studies

Ralph A. Dorner, M.D.,[*] Philip G. Keil, M.D.[†] (by invitation), and
Donald J. Schissel, M.D.[†] (by invitation)
Des Moines, Iowa

A NUMBER of authors[1, 2, 3] writing on the subject of pectus excavatum have questioned the existence of circulatory impairment from this deformity. Evans,[3] summarizing a study of 16 patients, aged 15 to 57 years (average age 24 years) stated, "It needs final emphasis that none of the 16 cases with depression of the sternum showed actual enlargement of the heart nor suffered from symptoms related to the heart. Indeed, they were all healthy and were handicapped only by the restrictions imposed on them by a medical examination that had misinterpreted the clinical and radiological signs." Steindler[4] concluded: "The operative elevation of the depressed sternum, as sometimes suggested, is a hopeless and unnecessary procedure." Sutton[5] feels cardiac disturbances do result from this deformity. The operative attack on the condition has continued.

Before The American Association for Thoracic Surgery, in 1938, Ochsner and DeBakey[6] reported a successfully treated case and presented an extensive review of the literature on this subject. The following year, Brown[7] suggested that the probable cause of pectus excavatum is anteroposterior shortening of the central tendon of the diaphragm. He presented surgical procedures for its prevention and alleviation. Sweet,[8] Ravitch,[9] Lester,[10] and others have attacked this problem applying the principles outlined by Brown. At the 1949 meeting Lester[11] reported 31 operated cases of thoracic cage deformities of diaphragmatic origin. Ravitch, reporting 8 cases in children 22 months to 10 years of age, listed the indications for surgery as (1) cosmetic, (2) orthopedic, and (3) physiologic. In these children cardiac disturbances were slight or absent. He concluded that surgical correction should be undertaken before general thoracic deformity or physiologic disturbances develop.

Most of the papers on this subject have dealt with surgical aspects of the problem, noting the fact that correction of the deformity was preserved and clinical improvement was maintained.

In this communication we wish to discuss a case of pectus excavatum having severe cardiac symptoms which were relieved by elevation of the sternum.

Sponsored by the Veterans Administration with the approval of the Chief Medical Director. Statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

[*] Attending Thoracic Surgeon.

[†] Department of Internal Medicine, Veterans Administration Hospital.

CASE REPORT

History.—L. S., a 28-year-old white male carpenter, entered the hospital April 11, 1949, complaining of palpitation (eighteen months' duration) and a chronic productive cough (six years' duration). Funnel chest deformity had been present since the age of 9 months. For eighteen months prior to hospitalization the patient had episodes of rapid regular heart action associated with weakness, dizziness, precordial pain, dyspnea, and sweating. The attacks occurred at irregular intervals, began and stopped suddenly, were produced by exertion and relieved by rest. They lasted two to fifteen minutes. During the attacks the pulse seemed regular but the rate increased to about 200 beats per minute. These episodes of tachycardia increased in severity and duration until two months prior to admission when slight exertion, such as assuming a standing position, initiated an attack.

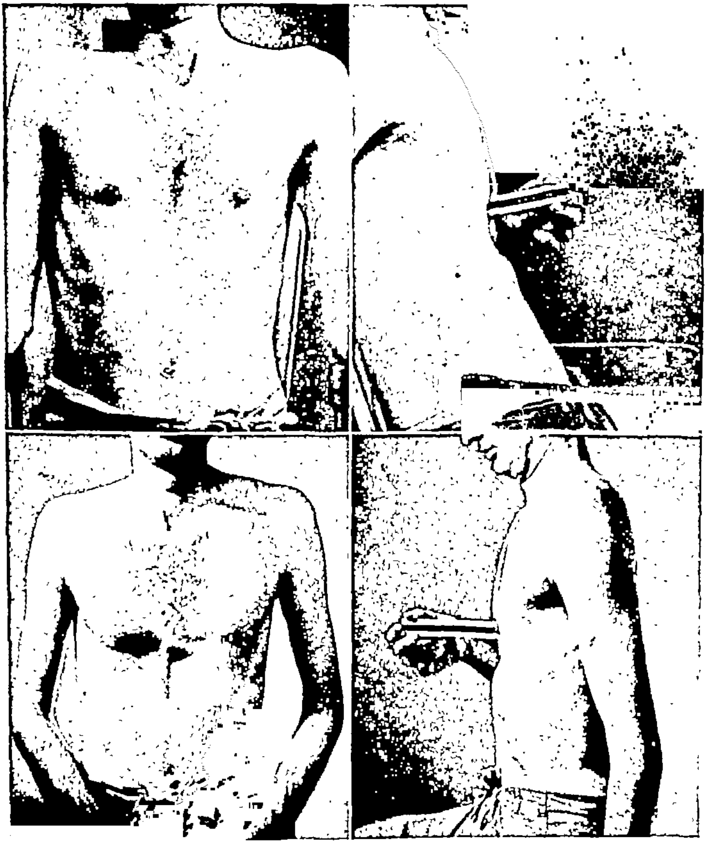

Fig. 1.—Anterior and lateral views of the chest, preoperative and postoperative.

The patient gave a history of moderately severe bronchiectasis for 6 years. There was no family history of funnel chest deformity. His father and mother were in good health and seven brothers and sisters were alive and well. The patient had lived a normal boyhood and was a distance runner on the high school track team. He was discharged from the army after eight months' service because of bronchiectasis.

Physical Examination.—The patient was 73 inches tall and weighed 136 pounds. The chest was long and thin and the lower sternum with adjoining cartilages was depressed two inches (Fig. 1). This depression held 300 c.c. of water. The trachea was in the mid-

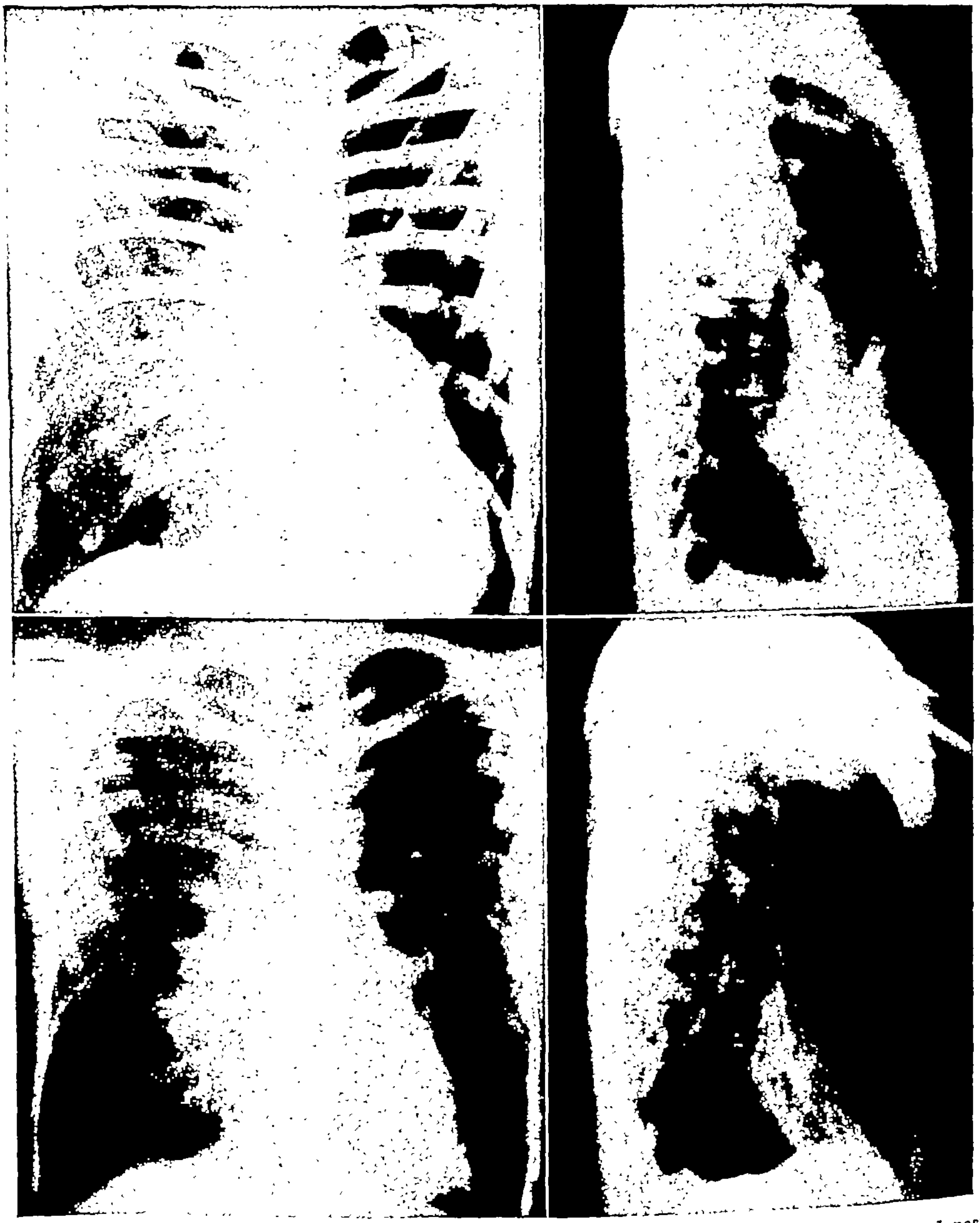

Fig. 2.—Posteroanterior and lateral roentgenograms of the chest, preoperative and postoperative. The normal dorsal curvature of the spine is absent. Clearance between the tip of sternum and the anterior surface of the vertebral bodies is one and three-fourths inches preoperatively and three and on-half inches postoperatively. Recession of sternum has not occurred by nine months after elevation.

line. The costal excursions were symmetrically limited. The normal curvature of the dorsal spine was absent. Expiratory wheezes were heard over the entire chest and coarse moist râles and rhonchi were present in both bases. The expiratory phase was prolonged. The heart was displaced to the left. The left border extended to the midaxillary line. The right border could not be localized. The heart tones were increased in intensity and there was a loud rumbling systolic murmur heard best in the fourth interspace to the left of the sternum. Blood pressure was 115/70. The heart rate varied from 68 at rest to 204 after minimal exertion.

Laboratory Examinations.—Urinalysis and complete blood count were normal. Serology was negative. The basal metabolic rate was plus 6. Sputum showed gram-positive cocci and numerous diphtheroids.

Posteroanterior and lateral chest roentgenograms showed marked indentation in the lower portion of the sternum and adjacent cartilages producing a marked funnel-shaped chest. The heart and mediastinum were displaced to the left (Fig. 2).

Bronchographic and bronchoscopic examinations revealed bilateral far-advanced bronchiectasis, most marked in the right middle and lower lobes.

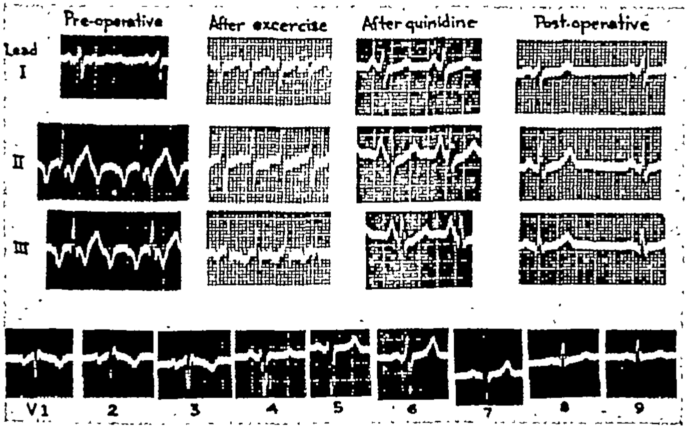

Fig. 3.—The electrocardiogram taken preoperatively under basal conditions (column 1) showed an auricular tachycardia with 3:1 auriculoventricular block, and deep, peaked inverted P waves in Leads II and III. A right heart strain pattern was present. After exercise (column 2) the block became 1:1 with a ventricular rate of 187. After the administration of quinidine (column 3) the rhythm became sinus and the right heart strain pattern persisted. Giant peaked P waves were striking.

Postoperatively the electrocardiogram became normal (column 4). The strain pattern disappeared. The P waves returned to within normal limits. The ventricular rate averaged 54.

"V" leads 1 through 9 before and after surgery were normal with the exception that they showed the heart to be definitely displaced and rotated to the left, the transition zone (septum) being at V_5 and V_6 (normal V_3 and V_4).

Hospital Course.—

Preoperative: Electrocardiograms showed the presence of a persistent supraventricular tachycardia with a varying block of 5:1 to 1:1 (Fig. 3). The 1:1 response occurred after minimal exertion and simulated the episodes of palpitation recorded in the history. After two weeks observation without change in the cardiac status, small doses of (0.2 Gm. every four hours) were administered orally and the rhythm reverted to after 0.6 Gm. However, the tall peaked P waves and the right heart

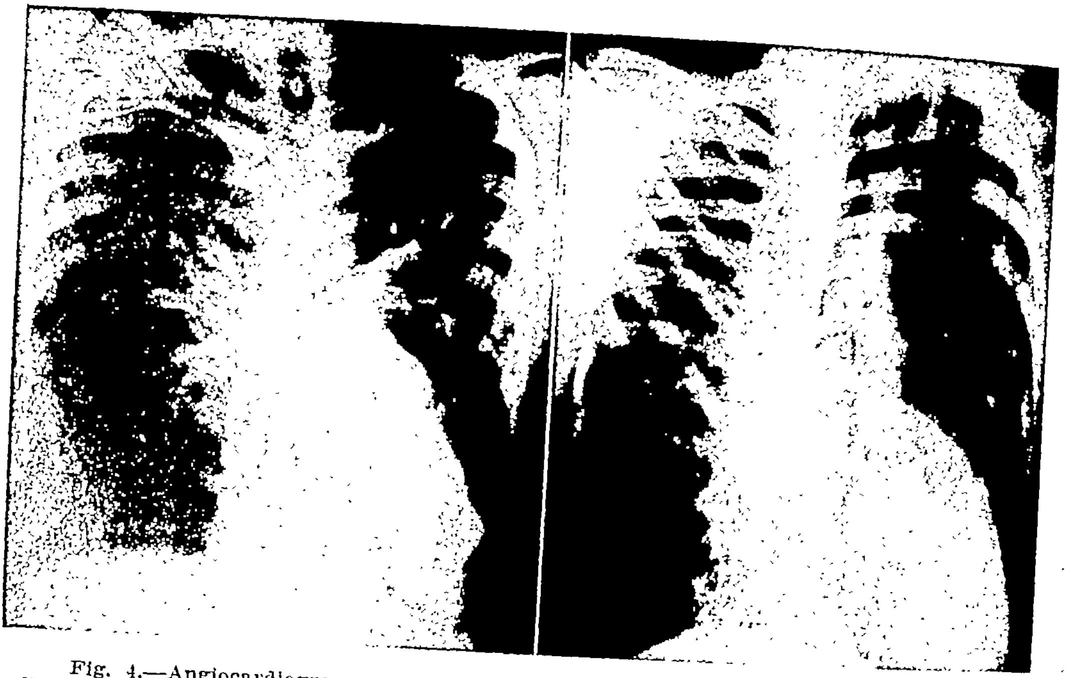

Fig. 4.—Angiocardiogram on the left taken in the posteroanterior position two seconds after rapid injection of 50 c.c. 70 per cent Diodrast into an antecubital vein. The superior vena cava is displaced to the left. The right atrium and ventricle are markedly dilated. The pulmonary artery makes up part of the left heart border. The angiocardiogram on the right was taken ten seconds after injection, in the left anterior oblique position. It shows a small posteriorly located left ventricle and hypoplastic aorta.

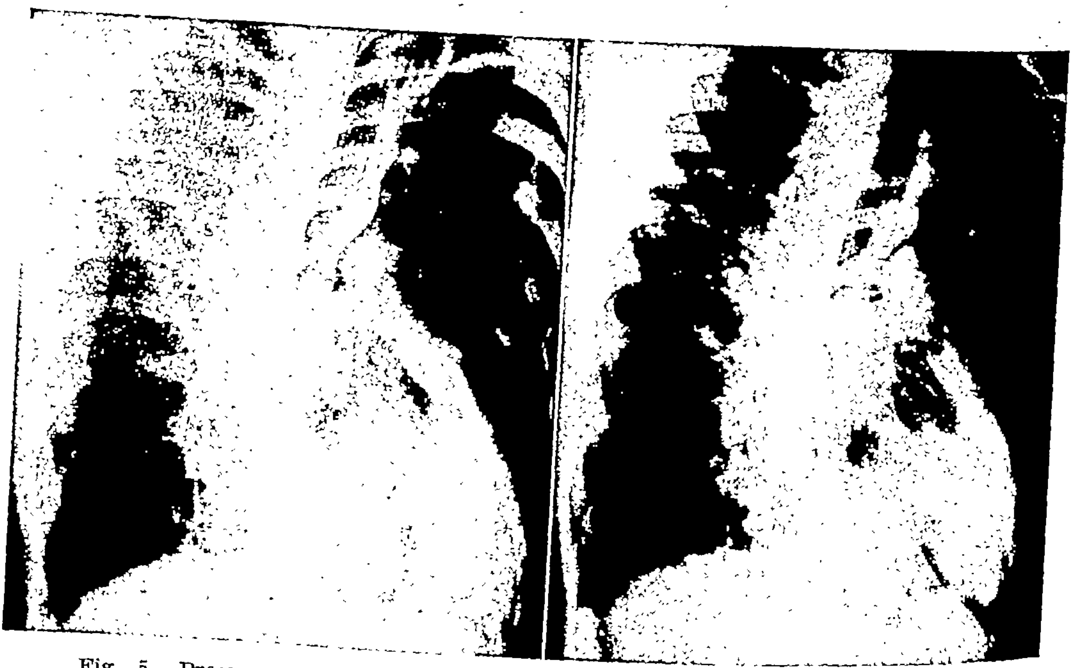

Fig. 5.—Preoperative angiocardiograms of the lesser circulation in the left anterior oblique position, taken four (left) and six (right) seconds after injection. The tricuspid valve ring appears distorted. There is obstruction to outflow of blood from the right atrium, which is normally free of dye on the four-second film.

sisted. The patient was dyspneic at bed rest before and after quinidine. He was raising 10 ounces of bronchiectatic sputum in twenty-four hours. During this time, treatment of the bronchiectasis consisted of postural drainage and penicillin therapy.

Angiocardiographic examinations preoperatively. (Figs. 4 and 5) showed marked enlargement of the right atrium and ventricle. The tricuspid valve ring was distorted. Dye puddled in the atrium, and circulation to the right ventricle was delayed. The greater circulation was normal. The aorta appeared somewhat hypoplastic.

Operative Procedure: On July 19, 1949, under nitrous oxide endotracheal anesthesia supplemented by sodium pentothal, a straight incision was made from the suprasternal notch to below the xyphoid. The skin, subcutaneous tissues, and pectoral muscles were reflected laterally on either side to beyond the costochondral junction from the second rib downward. The second to fifth cartilages (inclusive) were resected subperichondrally from sternal attachments to costal junctions, and the fused cartilages were divided. The intercostal muscles were left intact. The diaphragm was released by separating the xyphoid from the gladiolus, severing the substernal ligament. The sternum could then be brought well forward without dividing the manubrium and gladiolus (as recommended by most authors).

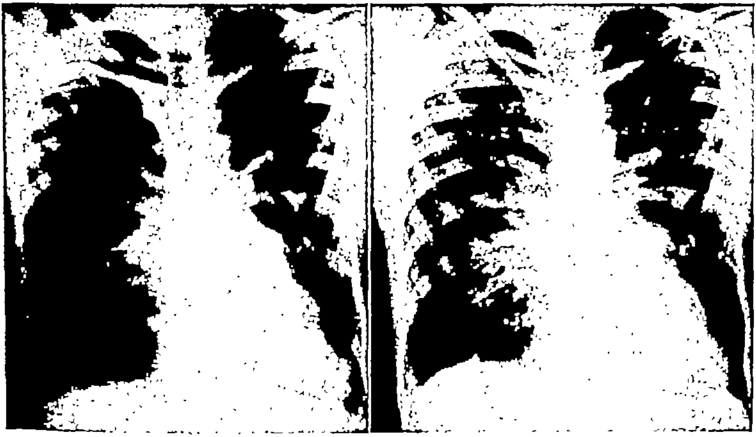

Fig. 6.—Angiocardiograms of the lesser (left) and greater (right) circulation three weeks after elevation of the sternum. The right atrium is considerably smaller and the circulation time is normal.

The xyphoid was allowed to drop posteriorly with the abdominal muscles and lower cartilages. A 10-inch segment of the left ninth rib was then resected subperiosteally and passed behind the sternum through the fourth cartilage spaces. When the rib was turned with its convexity anteriorly an over correction was obtained. However, when turned with its concavity anteriorly, the cosmetic effect was satisfactory.

After obtaining cancellous bone contact, the rib strut was anchored to the fourth anterior rib stump on either side with two interrupted sutures of No. 26 steel wire. With this fixation there was a tendency to spread the rib cage more widely, reducing the inversion of the distal portions of the ribs. The wound was flushed with normal saline and closed in layers without drainage after topical application of 300,000 units of penicillin onto the mediastinal tissues. No. 35 stainless steel wire sutures were placed in the fascia of the pectoral muscles as they were approximated. The skin and subcutaneous tissues were closed with interrupted sutures of similar material. The rib resection defect was closed with interrupted silk sutures. The operative time was two hours.

Postoperative: On return from the operating room, the patient was awake, the heart rate was 72, and the blood pressure 110/70. He was ambulated on the second postoperative day. The wound healed by primary intention.

Electrocardiograms obtained during the operative procedure showed diminution in the height of the P waves. The electrocardiogram taken the second postoperative day showed the right heart strain pattern had entirely disappeared and the P waves were normal.

Angiograms taken three weeks after operation showed (Fig. 6) the right atrium diminished considerably in size and the delay in the transit time of blood through the right atrium and tricuspid valve completely alleviated. Subjectively the dramatic response to sternal elevation paralleled the objective findings.

All studies have been repeated up to nine months postoperative and have remained within normal limits. The sternal depression now holds 30 c.c. of water. The murmur has disappeared.

DISCUSSION

Prior to elevation of the sternum, this patient was a cardiac cripple. The slightest exertion provoked tachycardia and incapacitating dyspnea. There had been no congestive failure. The type of arrhythmia, that is, supraventricular tachycardia with a varying degree of auriculoventricular block (5:1 to 1:1), is uncommon. The tachycardia had apparently been present for eighteen months and the degree of block varied with the patient's activity. The dynamics of the circulation were altered by delay of blood flow through the right atrium and tricuspid valve. This was obviated after sternal elevation. Disappearance of the murmur suggests that it had been due to distortion of the tricuspid valve. The previously conspicuous right heart strain pattern disappeared. Angiocardiograms obtained about three weeks after surgery showed considerable diminution in the size of the right atrium and a normal transit time of blood through the right heart. Postoperative exercise tolerance tests (Master's two step) were normal, in contrast to inability to carry out exercises preoperatively. The electrocardiogram became normal and has remained normal. In the nine months since surgery, there has been no recession of the sternum. Circulatory dynamics are normal. Though the heart size has diminished, the mediastinum is still shifted to the left and the transition zone is still V_5 to V_6 electrocardiographically.

SUMMARY

1. A case of severe funnel chest in a 28-year-old man with incapacitating cardiac symptoms and bilateral bronchiectasis is presented.

2. Detailed pre- and postoperative studies of the circulation bear out the premise that cardiac disability was due solely to impingement on the heart by the deformed sternum.

3. Results obtained by sternal elevation in this case substantiate the conclusions of Lester and Ravitch, who believe that surgical correction of severe or progressing deformities should be accomplished in childhood.

ADDENDUM

On June 5, 1950, a successful right middle and lower bilobectomy was performed for relief of this patient's bronchiectasis. The operative findings will be submitted for publication later.

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DISCUSSION

DR. J. E. DAILEY, Houston.—I was interested in the technique used by Dr. Dorner in this case, and how nicely it turned out. Last year, in discussing Dr. Lester's paper on pectus excavatum, I presented a case with a new technique, that of elevation and fixation of the sternum by a rib graft. I did not report the case because there were some individuals who questioned whether the result would hold up over a period of time. My patient disappeared and it was only last month that I discovered where she was located, about 225 miles away. With the fine cooperation of a doctor there, who made some x-ray and electrocardiographic studies and obtained a photograph, I received the following slides. I would like now to show the results after two years.

(Slides.) This shows the patient before operation, the lateral roentgenogram showing the marked depression of the sternum. The next shows the immediate postoperative photograph, and the next was taken about one month after operation. The lateral incision is where a portion of the ninth rib was removed. After removing the cartilage around both sides of the sternum, the sternum was elevated and the rib placed across beneath it between the second rib on the right and the third on the left, and wired in place, thus acting as a bridge and supporting the sternum in its proper position.

The next slide is the lateral roentgenogram taken two years after operation, showing an excellent distance between the sternum and the spine. The next slide shows what has happened to the rib graft and I think you can see clearly where it has completely fused with the ribs on both sides of the chest.

I believe that this example thoroughly illustrates that this technique is practicable and that it will stand the test of time as well as if not better than some others.

We did not have the complete and beautiful cardiographic studies on our case that Dr. Dorner and his associates had. However, I might add that our patient showed a marked right axis deviation by electrocardiography and had the same cardiac symptoms as did his patient before operation. One month after operation the electrocardiograph showed improvement, and was perfectly normal at the end of two years.

DR. LAURENCE MISCALL, New York.—To the many methods that have been advocated, recently was added in the literature the possibility of fixation of the elevated sternum by the use of Kirschner wires. I would like to show you one case in which we have used it and permit you to draw your own conclusions as to whether or not it is advisable.

(Slides.) This little girl came to the New York Hospital because of severe respiratory difficulty, and constantly held her hands against her sternum to give some stabilization for respiration. Here is the posteroanterior view, March 7, 1949, showing distinct displacement of the heart to the left. The lateral view shows the depression of the sternum.

At operation we did what has been advocated generally; resection of the costochondral junction with elevation of the sternum. This was fixed by the criss-cross insertion of two pieces of Kirschner wire which were drilled across the sternum from the normal level of about the second rib diagonally into the end of the sixth rib of the opposite side. One wire was removed on the sixth postoperative day because it presented under the skin. The next slide shows the lateral postoperative view. The posterior curvature of the longer wire indicates the presence of definite tension on it. This was an excellent method of stabilizing the sternum and we were quite satisfied with it at the time of operation. The patient made an uneventful recovery.

(Slide.) This roentgenogram was taken in early August, when the girl was at the beach with her family. To this time it was a very beautiful case presentation illustrating the use of a new method.

However, in October the child returned to the New York Hospital with the story from her mother that she had had whooping cough. She had absolutely no symptoms. When this patient was fluoroscoped, in full expiration the wire picked up the motion of the heart. I think you can see the evidence of pericardial effusion and the position of wire in this plate. It was necessary to approach this through the left pleural space in order to keep away from the previous repair of the sternum. We removed this foreign body from the child's pericardium which contained a large amount of blood.

I think you can draw your own conclusions as to whether you wish to place and leave such wires in a child's sternum.

DR. CHARLES W. LESTER, New York.—I have been very much interested in this demonstration of Dr. Dorner's, about the cardiac disability that occurs in cases of funnel chest. I am firmly convinced that all patients who have any degree of depression of the sternum, have some cardiac disability. This is manifest first by the fact that they are nearly all underweight, underdeveloped, and show the general condition of individuals who have chronic heart trouble. In the second place, they do not know that their heart action is restricted because they have never experienced normal heart action. They tell you they are all right before operation, but after operation they note a marked improvement. Of course in a case such as Dr. Dorner showed there is no question about the damage to the heart, and that is true in any case of marked depression. I have never known before what the mechanism was. We have made many electrocardiograms and they have never been distinctive; they show right axis deviation for the most part and many show abnormalities which the cardiologist cannot interpret.

Many of these children, and adults as well, are bothered by cough. Some go on to the extent of severe bronchiectasis, and at least three in my experience have had tuberculosis as well. I think this is probably due to the fact that the cough is ineffectual because of the narrow diaphragm. I thought at one time it might be due to a kink in the bronchus, but I think shortening of the diaphragm explains it better.

So far as the appliance goes for keeping the sternum up in place, the graft of a rib is a very ingenious method. However, I think that the ladder as originally described by Brown eleven years ago, if it curved somewhat, is the most satisfactory. The wires can be taken out completely, nothing is left in, and the sternum is nicely brought up. In most cases, especially if the patients are fairly young, that is, before the age of 5 years, there is no deformity that can be seen later on. In the older patients there may be some residual deformity which is proportional to the amount of irreversible deformity present at the time of operation.

DR. A. LINCOLN BROWN, San Francisco.—Dr. Dorner's case presentation certainly confirms the fact that there are cardiorespiratory changes in every case of funnel chest. Last year we suggested that we wished to get information by cardiorespiratory studies, as to when operation might be advisable and what, if any, results other than structural were obtained by operation. The first three cases studied indicated in the first place that there was reversion of improvement; in other words, a certain amount of improvement is noted after operation in the cardiorespiratory mechanism, but after about three weeks approximately 50 per cent of that improvement was lost. We tried to reason why. We believed it was due to the fact that we had made a fixation of the chest. That seemed to be the only thing that can happen in three weeks' time. During the first three weeks the chest is unstable and a certain amount of increased respiratory motion is present but, after that, organization and regeneration take place and fixation ensues, whereby some of the improvement is lost. Since then, no fixation of any kind has been used except the one at the proximal end of the sternum to elevate it. In fact, there has been intentional freeing of the rest of the thoracic cage to allow for increased respiratory motion to continue. Regeneration, so far as cartilage goes, is prevented. In these cases the improvement that took place, such as it was, has persisted.

One of the simplest of all tests to determine cardiorespiratory embarrassment is that of maximal breathing capacity. Preoperative studies show the great majority of our adult patients with funnel chest to have a maximum breathing capacity of less than 50 per cent of normal. Improvement in maximal breathing capacity after operation, approximately 35 per cent. In 11 cases, preoperatively we have found that 9 had definite symptoms; 8 of these cases showed variable abnormal electrocardiographic findings. These do not take into account axis deviation, which is practically to be expected as normal in these individuals. But the other abnormal changes all terminated, if they went long enough, in cor pulmonale. Postoperatively, we had 6 cases followed over twelve months with cardiorespiratory studies; 5 were improved, 1 was the same. Five showed an increase in maximum breathing capacity averaging 31 per cent, 1 was unchanged, and in all the electrocardiogram has remained essentially unchanged.

DR. DORNER (closing).—I feel very humble this afternoon. Most of what I know concerning pectus excavatum has been learned from the discussors of my paper. I should like to give Dr. Dailey credit: Last year I heard him report the use of a rib strut and it was because of this that I used a rib in our case. I would like also to acknowledge the fact that my co-authors were responsible for the clinical work-up of our case as described.

I think Dr. Miscall should be congratulated. The response of the audience to his remarks shows how much we appreciate an honest report whether the case turns out well or badly.

The only thing I can say about follow-up in our case is that angiocardiograms and electrocardiograms taken very recently show the continued improvement that we noted on the earlier slides.

In closing, I would like to thank the discussors for their remarks.

SURGICAL TREATMENT OF CORROSIVE STENOSES OF THE THORACIC PART OF THE ESOPHAGUS BY A SINGLE-STAGE PALLIATIVE ANASTOMOSIS

INTRACERVICAL RETROVASCULAR ANASTOMOSIS WITHOUT RESECTION OF THE ESOPHAGUS

VLADISLAV RAPANT, M.D.,* AND JAN HROMADA, M.D.†
OLOMOUC, CZECHOSLOVAKIA

IN THE treatment of corrosive strictures of the esophagus which fail to respond to dilatation, re-establishment of the continuity of the gastrointestinal tract can be accomplished by different methods. The reconstruction can be carried out within the thorax or on the chest wall. In the antethoracic reconstruction the major part of the esophagus is left in situ, and the communication between the pharynx, or the intact portion of the cervical esophagus, and the remaining part of the gastrointestinal tract is made by means of cutaneous, intestinal, gastric, or mixed tube.[1, 2, 3, 4] Another method of antethoracic reconstruction for high lying, extensive, benign stenoses of the esophagus is done in two stages. At the first stage a subtotal resection of the esophagus is done followed by establishment of a cervical esophagostomy and of a gastrostomy. At the second stage the stomach is transplanted into a subcutaneous, antethoracic tunnel and an anastomosis made between it and the superior segment of the esophagus. This principle was first employed by Rienhoff,[5] and later by Bigger[6] in a case of congenital atresia of the esophagus when primary anastomosis was not feasible, and then by Taylor[7] for carcinoma of the esophagus.

One disadvantage of all antethoracic procedures is the necessity for multiple stages which so greatly prolong the period of treatment. However, the chief disadvantage is that there is such uncertainty as to the results obtained. One of us (V. R.) performed successful antethoracic reconstructions in three patients by the method of Wullstein-Lexer with the period of treatment lasting an average of nineteen months. Furthermore, in one of these it was necessary to reoperate five years later because of stenosis at the site of the jejunodermal anastomosis.[8]

ADVANTAGES OF INTRATHORACIC RECONSTRUCTION OF DIGESTIVE TRACT

In intrathoracic reconstruction of the digestive tract the result is obtained in a single stage. According to the extent and location of the stricture one of two methods may be used. In the first, resection of the stenosed esophagus and end-to-end anastomosis is done.[9] In this procedure in order to prevent tension on the suture line, mobilization of the esophagus[10, 11] or of the cardia of the stomach must be done.[5] In another group of cases it will be necessary to mobilize the stomach so that it may be partly, or completely, transplanted into the thoracic cavity for anastomosis to the proximal segment of esophagus after resection of the strictured part, or of it and part of the stomach.[12, 13] The

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mobilized stomach may also be anastomosed to the partly mobilized esophagus above the site of stricture without resection.[14] As yet it has not been decided whether it is better to resect the entire strictured part of the esophagus, or to be content with a palliative anastomosis and leave the esophagus in situ.

DISADVANTAGES OF RESECTION OF THE ESOPHAGUS

There are a number of disadvantages in resecting the involved esophagus. (1) First is the difficulty in mobilizing the esophagus due to the extensive fibrotic changes in the esophagus and around it. At times it is impossible to do a complete excision.[12] (2) In stenoses involving the mid-portion and the upper third of the esophagus, the mobilization of this structure and of the aortic arch is sometimes followed by functional disorders which may cause the death of the patient.[15, 16] Garlock blamed the stimulation of the vagus nerves. Nissen denied this[17] but mentioned the appearance of asthmatic attacks in one of his patients. (3) The isolation of the esophagus in the region of the azygos vein may cause troublesome bleeding from it. (4) Injury to the thoracic duct may be caused and overlooked, and thus lead to the death of the patient. (5) Radical resection of the esophagus entails resection of the vagus nerves and this causes atony and dilatation of the stomach which is badly tolerated, especially if the anastomosis must be placed high in the chest or in the neck. The dilatation of the stomach frequently leads to compression of the lung with subsequent atelectasis, dyspnea, and coughing. Even though the chief etiological factor in the production of an esophageal peptic ulcer is removed by vagotomy such ulcers can still develop, as shown by Allison,[18] who observed the formation of an esophageal peptic ulcer in a patient a short time after vagotomy had been done for a gastric ulcer, and in four other patients after resection of the cardia for cancer. (6) Resection with anastomosis is always a lengthy procedure, particularly when a subtotal resection of the esophagus is done.

ADVANTAGES OF RESECTION OF THE STRICTURED ESOPHAGUS

The main advantage of the radical procedure is that it eliminates the possible formation of carcinoma on the basis of the previous corrosive damage to the esophagus, as was reported by Benedict.[10] He reported sixteen cases of carcinoma developing on the basis of corrosive lesions of the esophagus without subsequent stenosis. However, this factor cannot always be completely excluded as in some instances small pieces of injured esophagus have to be left in situ. The second advantage of resection is the elimination of possible stagnation of food below the site of anastomosis. This danger can be minimized, however, by doing the anastomosis immediately above the highest point of the stricture. Another advantage of resection is that it does away with the possibility of an abscess developing in the vicinity of the remnant of the strictured esophagus that has been left behind. But this is of theoretical importance only, as the changes in the strictured area are mainly fibrotic in character. It may be thought that the end-to-side anastomosis guarantees a better, and more permanent, patency than does the side-to-side anastomosis, but we feel that this is not true when the procedure is carried out properly, and it has not been true in our own experience. A definite answer to this particular point is not yet available. Finally, it is true that the end-to-side anastomosis is technically easier to perform than the side-to-side type.[12]

The feasibility of palliative side-to-side anastomosis in cases of stenosis of the middle and lower thirds of the esophagus is admitted by all. When, however, the stricture involves the upper esophagus the problem is far more complicated. Sweet[12] is of the opinion that a high anastomosis is not feasible without transection of the esophagus. We share this view in cases where the anastomosis is done by placing the stomach in front of the subclavian vessels.[20] If, however, contrary to Sweet's technique, the stomach is placed behind the vessels, the mere mobilization of the esophagus to the level of the aortic arch suffices for drawing the stomach into the neck and anastomosing it without tension. Because of these considerations, and as a result of our early success in the palliative side-to-side anastomosis for nonresectable carcinoma of the esophagus and cardia, we have decided to treat all our patients with corrosive strictures of the esophagus by this method.

In Table I is summarized our experience with seventy-two transthoracic operations for benign and malignant diseases of the esophagus, cardia, and stomach, during a period of somewhat less than three years. The marked difference in results from radical resection and from palliative anastomoses is apparent. Total gastrectomies were performed in twenty-four patients, twenty-three with carcinoma and one with a peptic ulcer. Four (16 per cent) of these

TABLE I. IMMEDIATE RESULTS OF TRANSTHORACIC OPERATIONS, RADICAL AND PALLIATIVE, FOR MALIGNANT AND BENIGN DISEASES OF THE ESOPHAGUS, CARDIA, AND STOMACH

OPERATION	NUMBER	DEATHS	
		NUMBER	PER CENT
Total Gastrectomy			
1. For peptic ulcer	1	0	0
2. For carcinoma of the stomach			
a. Simple: removal of both omenta and spleen	23	4	17.4
b. Combined: with resection of colon, pancreas, or liver	10	4	40
Total	34	8	23.5
Resection of Cardia and Esophagus			
3. For peptic ulcer of the cardia	4	1	25
4. For carcinoma of the cardia or lower fourth of the esophagus	17	6	35
5. For carcinoma of the middle part of the esophagus	3	0	0
Total	24	7	29
Palliative Anastomosis			
6. For carcinoma of the cardia and lower fourth of the esophagus	6	1	16.6
7. For carcinoma of the middle part of the esophagus	3	0	0
8. For benign stricture in the lower fourth of the esophagus	1	0	0
9. For benign stricture of the middle half of the esophagus	2	0	0
10. For stricture of the entire intrathoracic esophagus	2	0	0
Total	14	1	7.1

patients died. When resection of colon or pancreas was added to total gastrectomy the mortality rose to 40 per cent as four of the ten patients died. The combined immediate mortality for all total gastrectomies was 23.5 per cent. Resections were done in twenty-four patients for carcinoma of the cardia, and carcinoma of the esophagus. Seven of these died (29 per cent). Thus, of fifty-eight *patients who were subjected to radical transthoracic resections for lesions of the* stomach and the esophagus, fifteen died (26 per cent). Fourteen patients were treated by palliative transthoracic esophagogastrostomy, and only one died (7.1 per cent). These were done for nonresectable malignant stenoses of the cardia and thoracic esophagus, or for benign strictures of the thoracic esophagus.

Following these operations the patients are kept in the hospital for at least three weeks, as many of the common complications do not occur until after ten days. Sometimes at the beginning of the third week signs of leakage from the site of anastomosis appear, due to perforation of stitch abscesses, and later there develops mediastinitis and empyema. In Table I are included all deaths occurring in connection with the operations. The only death which occurred among the cases in which palliative anastomosis was done was in a man who had a stenosing carcinoma of the cardia involving the esophagus with metastases to the liver and peritoneum. It is felt that in this patient too much surgery was done.[21] However, we feel strongly that where radical resection can be done for carcinoma it should be done, even though the mortality rate is higher than for palliative *anastomosis. In this opinion we differ from* d'Allaines and Dubost.[23]

I. ESOPHAGOGASTROSTOMY WITHOUT RESECTION FOR CORROSIVE STRICTURES OF THE MID-PORTION OF THE ESOPHAGUS

Two patients with stenosis of the mid-portion of their esophagus resulting from the ingestion of lye were treated by esophagogastrostomy without resection of the esophagus. In both the stomach was mobilized through an abdominal approach, the right crus of the diaphragm divided, and then through a right thoracic approach a side-to-side anastamosis was performed.

CASE 1.—The first patient was a 30-year-old woman who had swallowed some lye, by mistake, ten years before being seen. Because of increasing difficulty in swallowing she had had a gastrostomy done nine years previously. Roentgen-ray examination revealed a stenosis starting somewhat above the level of the bifurcation of the trachea, and continuing down to the cardia. The stomach appeared to be normal. On April 28, 1949, operation was done under endotracheal, ether-oxygen anesthesia, supplemented by curare. Through a supraumbilical incision with resection of the xyphoid process, the gastrostomy was first closed and then, the stomach and lower 4 cm. of the esophagus were mobilized. The right crus of the diaphragm was divided obliquely, and the abdominal wall was then closed. The patient was then turned on the left side and the right pleural cavity entered through the bed of the sixth rib, which had been subperiosteally resected. A small paravertebral segment of the fifth rib was also resected. The phrenic nerve was not crushed. The azygos vein was divided and then the esophagus above the site of the stenosis was freed of overlying tissue but not mobilized. After division of the inferior pulmonary ligament, and of the mediastinal pleura, the lower 8 cm. of the esophagus was mobilized. The posterior wall of the mobilized stomach was then anastomosed to the anterior wall of the esophagus above the stenosis, and the stomach anchored to the pleura and diaphragm. A rubber tube drain was placed into the pleural cavity through the ninth intercostal space, and the chest wall closed in layers. Recovery was prompt. Roentgen-ray examination on the fourteenth day after operation (Fig. 2) showed a well-functioning anastomosis at the level of the bifurcation of the trachea. There was evidence of slight hastening of the emptying of the stomach. On May 18 she was discharged as cured, being able to swallow solid food without trouble. By June 27 she had gained two kilograms in weight and had remained well.

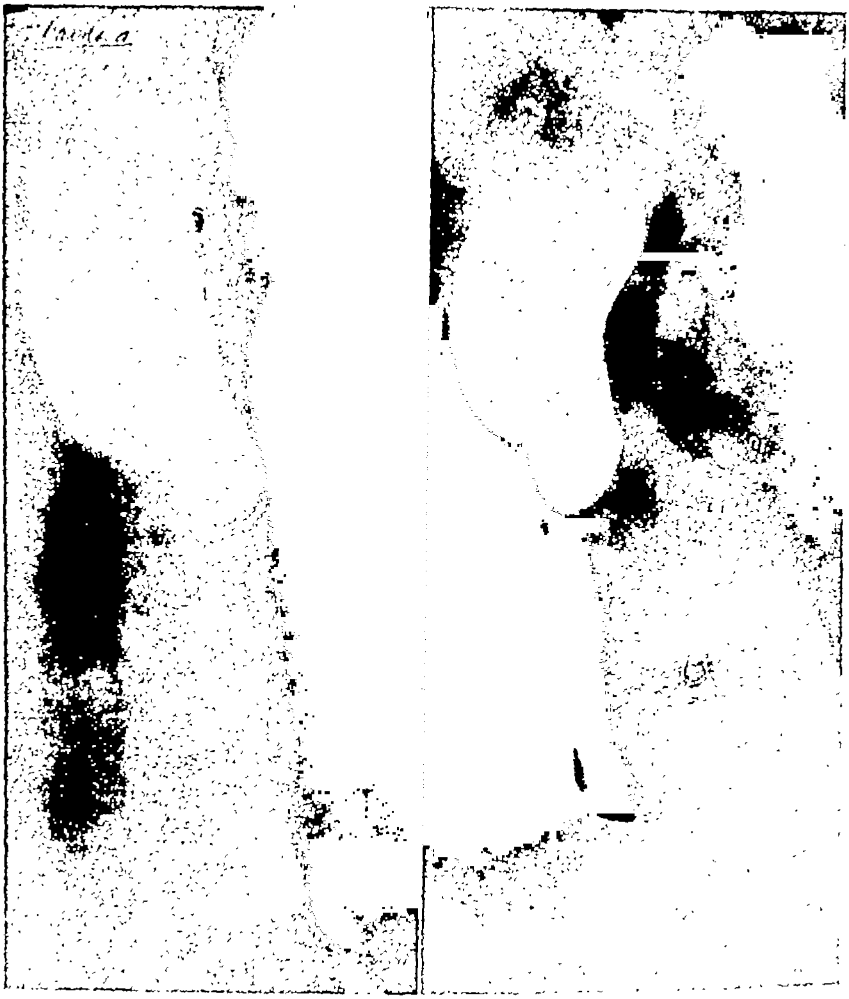

Fig. 1 (Case 1).—Preoperative roentgenogram of stenosis of the middle half of the esophagus.

Case 2.—The second patient was a 26-year-old woman who had swallowed lye, by mistake, thirteen years before admission to the hospital. Difficulty in swallowing had become so severe in a few weeks that dilatations of the esophagus had been started. These dilatations were continued at intervals, but during the last six months she had only been able to swallow semisolid food. She had lost ten kilograms in weight. Roentgen-ray examination showed the stenosis to be above the level of the bifurcation of the trachea with dilatation of the esophagus above it. On May 25, 1949, she was operated upon in a manner exactly similar to that used in the first case. Both the vagi and the phrenic nerve were preserved intact. Recovery was uneventful and she was discharged on the seventeenth day swallowing solid food without difficulty. Roentgen-ray examination revealed patency of the anastomosis.

DISCUSSION

As in carcinoma of the esophagus, so, with corrosive stenosis of the esophagus, the operative technique will vary with the location and extent of the stenosis. This is as true of the radical procedures as of the palliative anastomosis. For stenosis of the lower fourth of the esophagus there is no question about the advisability of the approach through the left chest. There is some question, however, as to whether it is better to use the stomach, or a jejunal loop as prepared by Roux and suggested by Allison.[24] The suggested advantage of using a structure nearer to the size of the esophagus for anastomosis to it, and the possible elimination of esophageal peptic ulcers by using the jejunal loop, are balanced or outweighed by the greater operative risk and the elimination of the stomach from the direct intestinal channel.

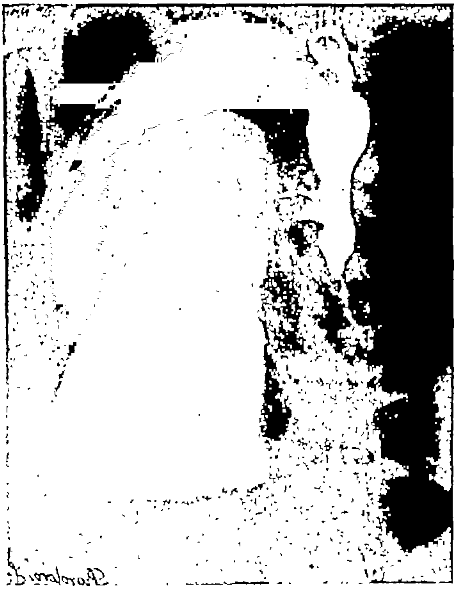

Fig. 2 (Case 1).—Postoperative roentgenogram of intrathoracic anastomosis through right thoracotomy taken fourteen days postoperatively.

In stenoses of the middle third of the esophagus there will be difference of opinion as to choice of approach. This will be particularly true when the stenosis starts immediately below the arch of the aorta, or behind and above it. When the anastomosis can be done below the arch of the aorta a left thoracic approach is to be preferred as it eliminates the need for a preliminary mobilization of the stomach through the abdomen. For anastomoses above the arch of the aorta we believe that transabdominal mobilization of the stomach according to the technique of Macmanus, followed by a right thoracotomy will be better.[22] This has been our experience with palliative anastomosis in inoperable cases of carcinoma located behind and above the arch of the aorta. The right-sided approach allows easier access to the esophagus, avoids injury to the thoracic duct, and the damage to the diaphragm is minimized. In our opinion these advantages outweigh the disadvantage of the preliminary laparotomy.

II. INTRACERVICAL ESOPHAGOGASTROSTOMY

The indications for intracervical esophagogastrostomy are as follows: (1) Malignant growths in the upper fourth of the esophagus where intrathoracic anastomosis is not feasible because of the high location of the tumor, or where the neoplasm is located too low for the restoration of the alimentary canal by the method of Wookey. (2) In those congenital atresias of the esophagus where, after closure of the tracheoesophageal fistula, reconstruction of the continuity of the esophagus will be impossible and a gastrostomy and esophagostomy will be needed.[20] It is highly probable that the antethoracic implantation of the stomach into a subcutaneous tunnel as described by Rienhoff[5] will be safer. (3) Benign stenoses of the esophagus of cicatricial origin which affect practically all of the organ.

The first intracervical esophagogastrostomy, of which we know, was performed by Sweet in June, 1947. The patient was a 21-month-old child with a tracheoesophageal fistula which was closed at the first-stage operation, and at the second stage the anastomosis was completed. On Oct. 28, 1947, one of us (V. R.) had the honor of being present at an operation for carcinoma of the upper esophagus when Sweet performed a subtotal resection of the esophagus and a subsequent intracervical esophagogastrostomy. The patient made a prompt recovery. Soon afterward Garlock[15] published his technique for intracervical anastomosis after subtotal resection of the esophagus for carcinoma high above the aortic arch. His patient died on the second day after operation, probably as a result of profound functional changes due to stimulation of the vagus nerves. Subtotal resection of the esophagus is common to both methods, the principal difference being that in performing the anastomosis Garlock brings the stomach up behind the aortic arch and its branches whereas Sweet brings the stomach up in front of them. In both methods the vagi will be stimulated. Moreover, in Sweet's method there will be an additional stimulation of the periadventitious nervous plexuses, and perhaps even a stimulation of the carotid sinus. The tachycardia following change of position in Sweet's patient during the first four days after operation was ascribed to increased activity of the carotid sinus.

When considering the methods of single-stage operations which would be of the greatest advantage to our two patients with corrosive stenosis of the entire esophagus our aims were threefold. First, we wished to abandon the technically difficult and physiologically severe mobilization of the strictured esophagus with subsequent subtotal resection. Then we wished to transpose the mobilized fundus of the stomach behind the great vessels in the chest and in the neck, thereby producing as physiologic a course for the new esophagus as possible. Finally we wished to reduce, as much as possible, the disturbances caused by neurovegetative stimulation. It was necessary, therefore, by studies on cadavers, to decide which anatomic structures are encountered during the performance of retrovascular transposition of the stomach.

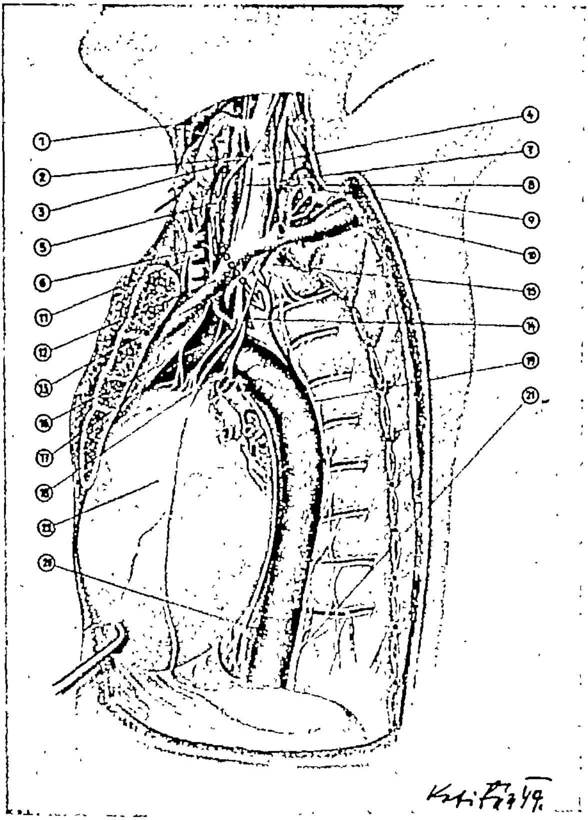

Fig. 3.—Illustrating the neurovascular cervical trunk and the mediastinal organs on the left side.

1, Superior thyroid vessel; *2*, ansa hypoglossi; *3*, common carotid artery; *4*, internal jugular vein; *5*, esophagus; *6*, recurrent nerve; *7*, phrenic nerve; *8*, vagus nerve with right cardiac; *9*, brachial plexus; *10*, clavicle; *11*, trachea; *12*, innominate vein; *13*, thoracic duct; *14*, esophagus; *15*, stellate ganglion; *16*, aortic arch; *17*, sympathetic cardiac nerve; *18*, recurrent nerve; *19*, truncus sympaticus; *20*, esophagus with left vagus nerve; *21*, major splanchnic nerve; *22*, pericardial sac.

ANATOMIC REMARKS

The structures which will be encountered during the preparation of the retrovascular tunnel in addition to the esophagus itself are: the thoracic duct, the stellate ganglion and its branches, the longitudinal septum, and the cover of the pleural dome (Fig. 3).

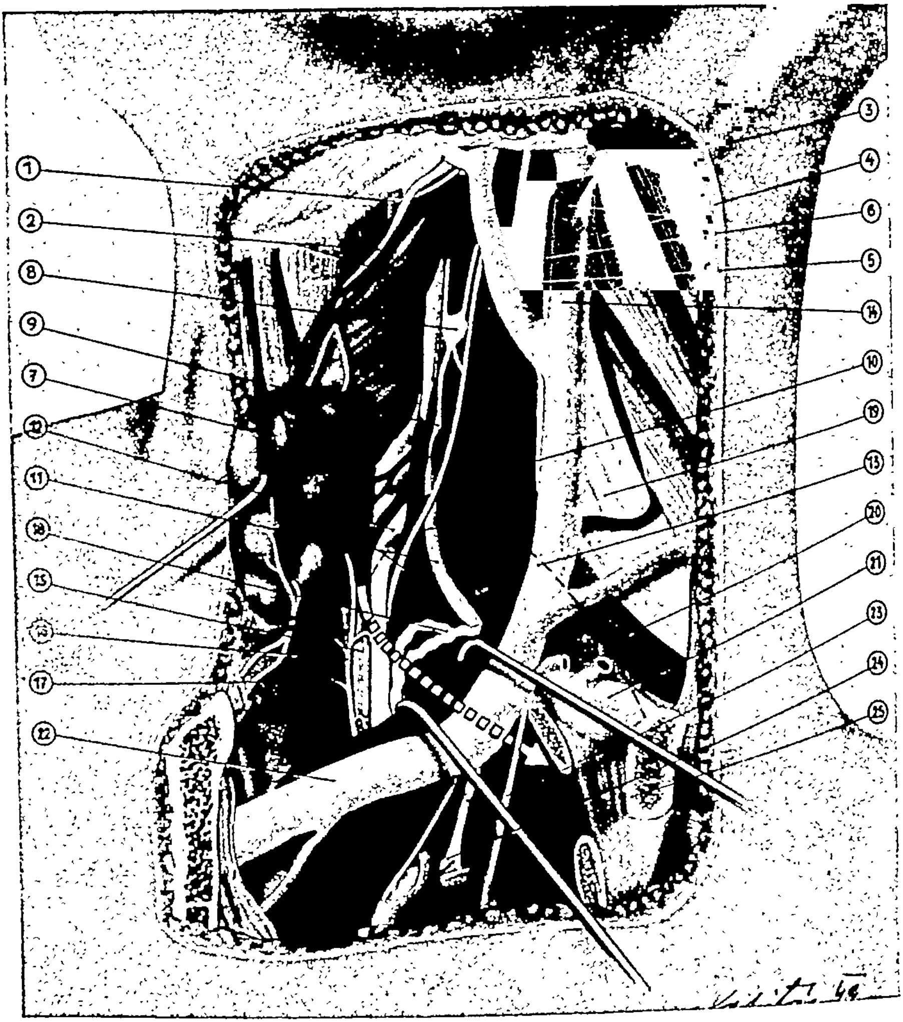

Fig. 4.—Showing the operative site on the neck. Neurovascular cervical trunk removed from the fibrous sheath.

1, Superior laryngeal nerve; *2*, superior thyroid vessel; *3*, right descending hypoglossal nerve; *4*, cervical plexus; *5*, common carotid artery; *6*, vagus nerve; *7*, thyroid gland; *8*, medial sympathetic ganglion; *9*, intermediate left ganglion; *10*, inferior thyroid artery; *11*, vertebral vessel; *12*, longitudinal septum; *13*, cupula of the pleura; *14*, internal jugular vein; *15*, esophagus; *16*, recurrent nerve; *17*, trachea; *18*, thoracic duct; *19*, brachial plexus; *20*, subclavian artery; *21*, subclavian vein; *22*, innominate vein; *23*, phrenic nerve; *24*, recurrent nerve; *25*, clavicle.

The thoracic duct runs first in the chest between the azygos vein and the aorta. At the level of the fifth thoracic vertebra, corresponding to the level of the bifurcation of the trachea, it crosses to the left side through areolar tissue behind the esophagus, and runs up posterior to the arch of the aorta and accompanies the left subclavian through the thoracic inlet into the neck. In the neck the thoracic duct appears in the fissure between the common carotid and subclavian arteries, forming an arch with its convexity upward, and crosses in front of the subclavian artery, vertebral artery and vein, and the thyrocervical trunk or its branches, and empties into the vascular system at the angle of junction between the subclavian and internal jugular veins. In establishing the retropleural and retrovascular tunnel for the upward passage of the fundus of the stomach the thoracic duct and the entire neurovascular trunk are shifted together (Figs. 4 and 6).

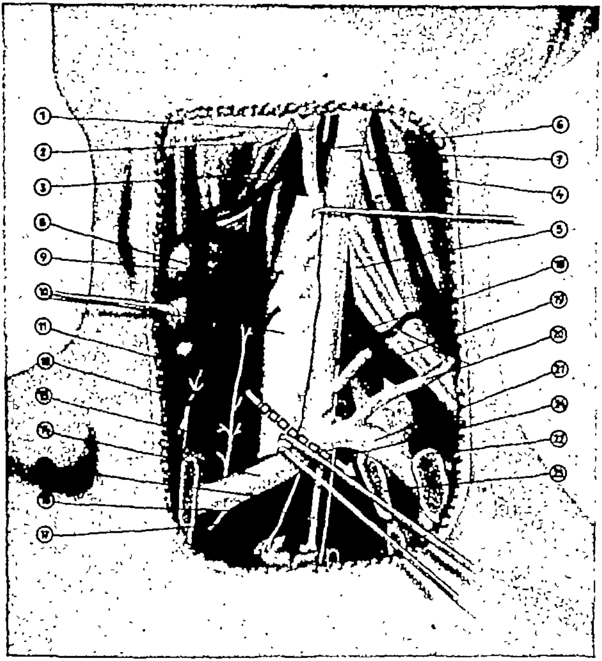

Fig. 5.—Showing the operative site on the neck. Neurovascular cervical trunk is covered from the medial side partially by the fibrous sheath. Arrow demonstrates the direction and the course of the retrovascular tunnel.

1, Right descending hypoglossal nerve; *2,* superior laryngeal nerve; *3,* superior thyroid vessel; *4,* cervical plexus; *5,* brachial plexus; *6,* carotid artery; *7,* internal jugular vein; *8,* thyroid gland; *9,* right inferior artery of the thyroid gland; *10,* longitudinal septum; *11,* recurrent nerve; *12,* trachea; *13,* esophagus; *14,* innominate vein; *15,* aortic arch; *16,* right cardiac vagus nerve; *17,* vagus nerve; *18,* phrenic nerve; *19,* subclavian artery; *20,* superficial cervical vessel; *21,* subclavian vein; *22,* clavicle; *23,* first rib; *24,* internal thoracic artery.

The stellate *ganglion* and the *entire sympathetic trunk are not in immediate* contact with the region of the retrovascular tunnel. Nor does the stomach, when anastomosed to the esophagus, come into direct contact with the ganglion and sympathetic trunk. The *only structures* that come into close *proximity* to the operative site are the visceral branches of the stellate ganglion to the cupula of the pleura, the esophagus and trachea, and the inferior cardiac nerve. The inferior cardiac nerve first runs along the posterior aspect of the common carotid artery, then behind the arch of the aorta and on to join the cardiac plexus. As it is common for vegetative nerves to have anomalous courses, their fibers may be damaged by the pressure of the transposed stomach on the posterior aspect of the chest. Bruising these fibers might explain the tachycardia which was noted during the first days after operation, if this tachycardia were not simply due to the long and severe operative procedure.

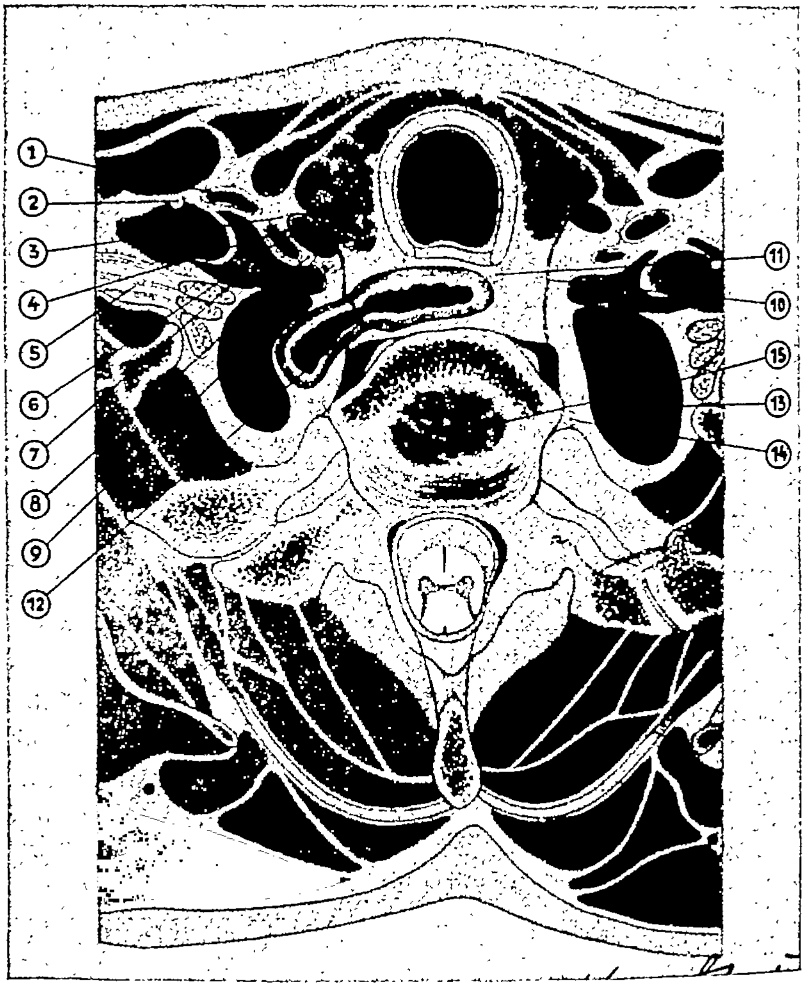

Fig. 6.—Section through the neck in the level of the anastomosis.

1, Left subclavian vein; *2*, phrenic nerve; *3*, right descending hypoglossal nerve; *4*, common carotid artery; *5*, brachial plexus; *6*, internal jugular vein; *7*, left subclavian artery; *8*, vagus nerve; *9*, thoracic duct; *10*, longitudinal septum; *11*, recurrent nerve; *12*, anastomosis between esophagus and fundus ventriculi; *13*, cupula of the pleura; *14*, truncus sympathicus; *15*, first thoracic vertebra.

The longitudinal septum (Figs. 5 and 6) is part of the connective tissue investment of the cervical neurovascular trunk. It is also most distinctly developed within the chest. In the neck it is formed by the pulsatory effects of the carotid artery on the surrounding, originally structureless, connective tissue. The dorsal part of the septum which extends from the fibrous sheath to the prevertebral fascia, and the ventral part which is directed towards the middle cervical fascia, are considerably attentuated and may be altogether absent, particularly in the anterior portion. The middle part of the septum, which is the thickest, is pierced by branches of the inferior thyroid artery which pass to the thyroid gland or to the esophagus. The longitudinal septum extends inferiorly in the chest to become continuous with the suspensory ligament of the diaphragm. Like all cervical fascia, the longitudinal septum shows individual variations as far as its development and condensation are concerned, but it is well developed in the region of the neurovascular trunk and serves as a good protection against injuries during the preparation of the retrovascular tunnel (Fig. 6).

The cupula of the pleura reaches posteriorly to the neck of the first rib (Fig. 4). It is covered by a layer of connective tissue belonging to the endothoracic fascia, and is bridged by the suprapleural fascia of Sibson.

OPERATIVE TECHNIQUE

1. *First step of the Operation: Thoracic procedure.*—With the patient lying on the right side, left thoracotomy through the bed of the previously resected eighth rib is done. After resection of the intercostal nerve, the corresponding *vessels are transfixed at both ends of the incision. After allowing the lung to* collapse, 10 c.c. of 1 per cent procaine without epinephrine are injected into the pericardial sac. The same solution is used for infiltration of the thoracic sympathetic chain, the splanchnics, and the mediastinum. The inferior pulmonary ligament is divided and the bleeding points controlled by electrocoagulation. The mediastium is entered and the leaves of the pleura are reflected to allow visualization of the esophagus. By blunt, and, where necessary, sharp dissection the lower part of the esophagus is then delivered from the mediastinum.

After crushing the phrenic nerve for a distance of 2 mm. the diaphragm and esophageal hiatus are divided between transfixion sutures, after which clips are applied. This procedure facilitates the closure of the diaphragm after the termination of the thoracic stage of the operation. Before mobilizing the stomach the patency of the pylorus is determined. The stomach is then mobilized in the usual manner, preserving the right gastric and gastroepiploic arteries and leaving the spleen in situ.

After the stomach and cardia are freed the esophagus is mobilized to the level of the aortic arch. All bleeding is carefully controlled and injury to the vagus nerves is avoided. In our first case both vagi were severed as it was feared that intracervical transposition of the stomach could not be otherwise accomplished. *In the second case only the anterior branch of the vagus could* be identified but it was preserved. Through the wall of the fundus of the mobilized stomach are passed two guide sutures of silk, and then by means of a Reverdin needle they are brought out through the second interspace in the midclavicular line.

The next step is fixation of the stomach to the posterior chest wall with interrupted sutures. This is done by starting at the prepyloric part and proceeding upward to the fundus, anchoring the stomach along its greater curvature to the parietal pleura and along its lesser curvature to the mediastinal pleura. Fixation of the diaphragm to the gastric wall and closure of the diaphragm then follow. Before closing the thoracotomy wound a drain is placed in through the ninth intercostal space in the posterior axillary line.

2. *The Second Step of the Operation: Intracervical Anastomosis.*—The patient is placed on his back and about fifteen or twenty minutes are allowed for stabilization of the patient's pulse and blood pressure.

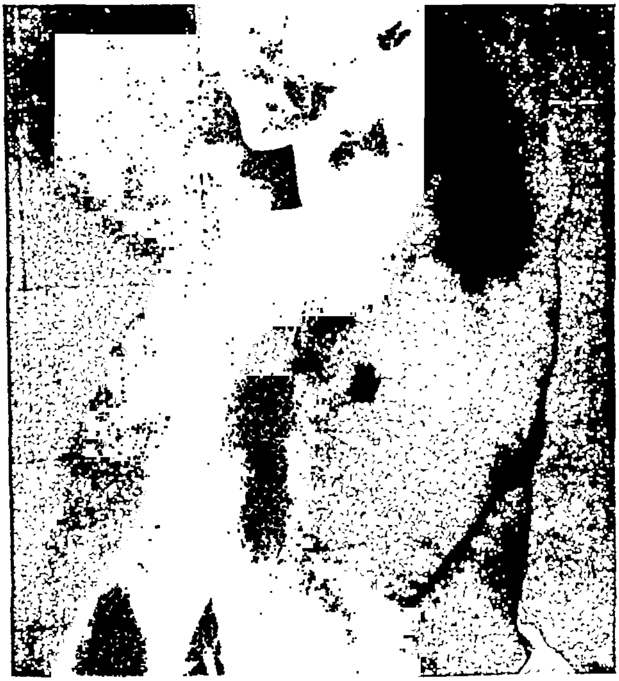

Fig. 7 (Case 3).—Incisions for the first and second steps of intracervical anastomosis.

Incision: The incision is made along the inner border of the sternomastoid muscle from the thyroid cartilage to the clavicle, the lower end of the incision being about 1 cm. lateral to the sternoclavicular joint. The incision is extended downward to the second intercostal space. Immediately above the upper border of the third rib the incision is curved slightly laterally to the point at which the guide sutures from the stomach emerge (Fig. 7).

Temporary resection of the clavicle and resection of segments of the upper two ribs. After preparation of the lateral musculocutaneous flap the clavicle is denuded and muscular insertions stripped. After dividing the sternal part of the sternomastoid muscle the clavicle is divided extraperiosteally with a Gigli saw at a point about 5 to 6 cm. from the sternoclavicular joint. In both of our cases we then dislocated the clavicle at the joint but we believe that it would be better to divide the clavicle outside the joint so as not to disturb it. The pectoralis major muscle is next divided along the course of its fibers, and then

part of the sternomastoid muscle is sutured and the pectoralis major muscle reunited. The closure of the wound is completed without drainage. The lung is then re-expanded after the injection of 25,000 units of penicillin and 0.5 Gm. of streptomycin into the pleural cavity and the tube drain into the cavity closed. The final step is the performance of a paravertebral block.

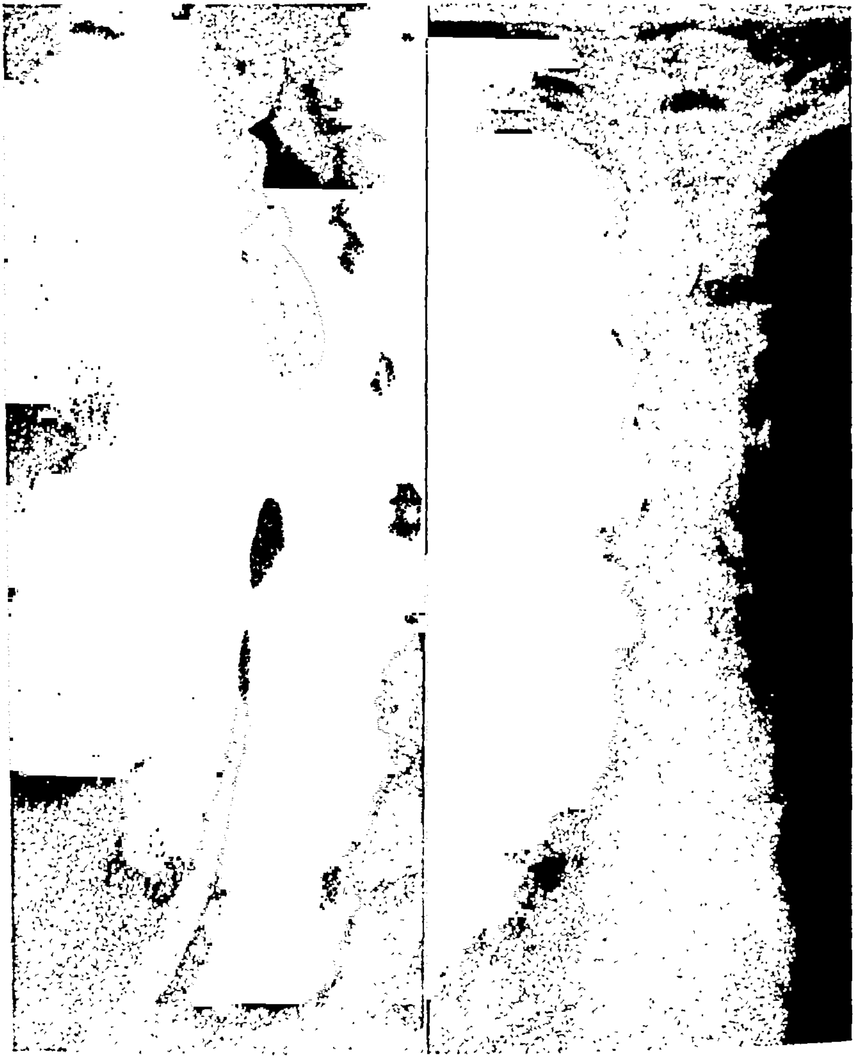

Fig. 8 (Case 3).—Preoperative roentgenogram of high stenosis of the esophagus.

Postoperative treatment.—This does not differ from the postoperative treatment after resection, or palliative anastomosis, for carcinoma of the esophagus or cardia. Twelve hours after operation the patient is started on clear tea, 30 c.c. every two hours. The quantity of fluid is gradually increased so that the patient is taking liquids freely on the fourth day. After the sixth day he is given semisolid food which is always followed by tea. At the end of a fortnight the patient is on full diet.

The fluid in the thorax is evacuated every twenty-four hours. As soon as the fluid stops forming and the lung has re-expanded the drain is removed. In the first case this was done on the second day, and in the other case it was done on the third day. After aspiration of the pleural fluid there is always injected into the thorax 25,000 units of penicillin and 0.5 Gm. of streptomycin.

Pain is relieved by paravertebral block. Recently we have obtained good results with a drip infusion of a 0.2 per cent solution of procaine in 5 per cent dextrose as described by Brittain.[27]

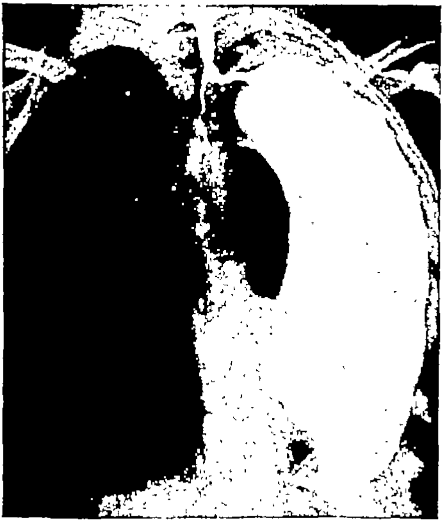

Fig. 9 (Case 3).—Postoperative roentgenogram of intracervical retrovascular anastomosis taken twenty-one days postoperatively.

Complications.—The only complication which occurred in our cases was a considerable dilatation and atony of the stomach which occurred in the first patient who had had both vagi severed. Dyspnea was caused and the patient was greatly troubled for a fortnight. Relief was obtained from repeated aspiration of the gastric contents. In both patients tachycardia was observed during the first postoperative days, disappearing on the third and fourth days, respectively. This symptom was ascribed to the severity of the operation rather than to stimulation of the cardiac nerves. No circulatory changes in the left upper extremity were noted. There were no pulmonary complications and the wounds healed by primary intention.

REPORT OF CASES OF INTRACERVICAL GASTROESOPHAGOSTOMY

Case 3 (J. S.).—This patient was a 35-year-old woman who drank lye, by mistake, in 1937. After about two months her difficulty in swallowing required esophageal bouginage, which she was later able to do to herself. One such performance, in 1947, was followed by a febrile reaction, accompanied by chest pains. After subsidence of the symptoms further decrease in the esophageal patency occurred so that, from that time, she only could swallow liquids although bouginage was repeated at regular intervals. On roentgen-ray examination it was seen that she had a constriction of esophagus starting at the sternoclavicular joint (Fig. 8).

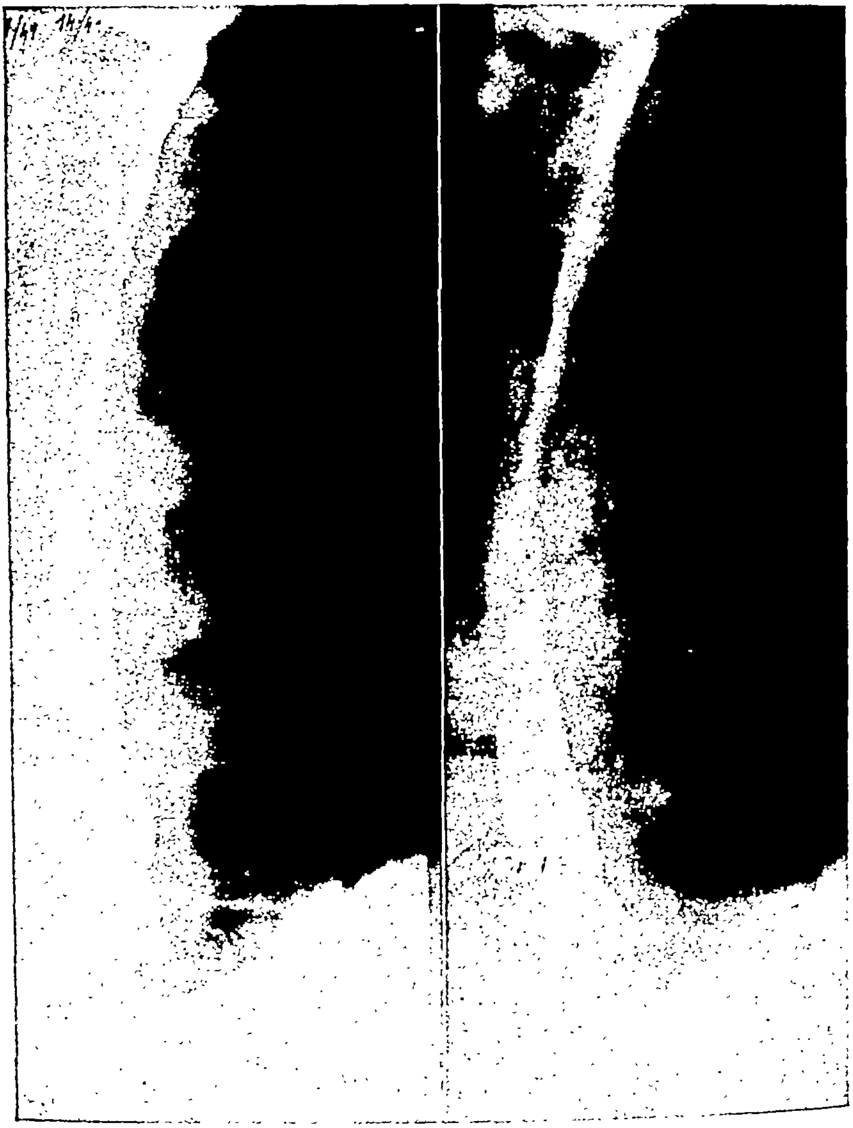

Fig. 10 (Case 4).—Preoperative roentgenogram of high stenosis of the esophagus.

On Nov. 2, 1948, she was operated upon under endotracheal ether-oxygen anesthesia with curare. Intracervical esophagogastrostomy was carried out according to the method just described. As the esophagus showed fibrous changes, especially in the middle portion, it was feared that it could not be mobilized sufficiently to allow the stomach to be brought up into the neck unless the vagi were severed. The nerves were easily found on the lower third of the esophagus and were divided. The postoperative course was complicated by gastric atony and dilatation as noted previously. By November 27, she was cured and was discharged in good condition. Follow-up examination on Aug. 7, 1949, showed that she had no difficulty in swallowing and had gained seven kilograms in weight. She was troubled with meteorism, and diarrhea alternating with constipation. The roentgen rays showed that the anastomosis was functioning well but that the atony and dilatation of the stomach had continued (Fig. 9).

CASE 4.—G. K. was a 24-year-old man who ingested lye by mistake six months prior to the writing of this paper. After subsidence of the first symptoms he began to have difficulties in swallowing which rapidly grew worse in spite of regular bouginage. He was only able to swallow semisolid food and lost thirteen kilograms in weight. He refused any further attempts at dilatation and requested operation. Roentgen rays showed evidence of stenosis apparently involving most of the thoracic esophagus (Fig. 10). On April 24, 1949, he was operated upon under intratracheal, ether-oxygen anesthesia, according to the method described previously. The anterior vagal trunk was preserved. Postoperative course was without complications and he was discharged on May 21, 1949, swallowing well. Roentgen rays showed the anastomosis to be functioning properly (Fig. 11).

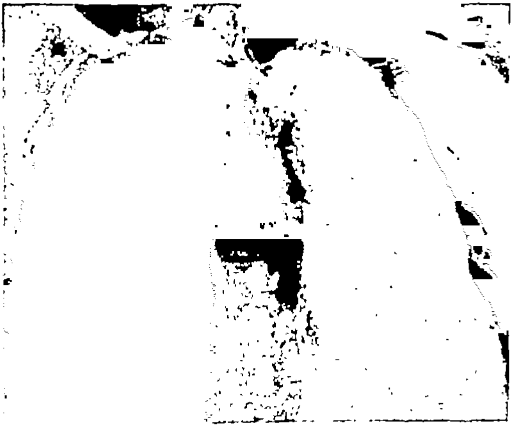

Fig. 11 (Case 4).—Postoperative roentgenogram of intracervical retrovascular anastomosis taken fifteen days postoperatively.

SUMMARY

In corrosive stenoses of the thoracic esophagus patency can frequently be effected by surgical means. One may do an antethoracic plastic reconstruction, or an intrathoracic or intracervical anastomosis.

The antethoracic procedure has the disadvantages of the need for multiple stages to achieve the desired end result, and the uncertainty of the result being satisfactory. *On the other hand the use of an intrathoracic, or intracervical,* anastomosis makes possible the achievement of the desired result in one stage.

As in carcinoma of the esophagus, extent and location of the corrosive stricture must be considered separately. As far as the extent is concerned, it will only rarely be possible to resect the stenosed area and do an end-to-end anastomosis of the esophageal segments. In the great majority of cases the re-establishment of the continuity of the digestive tract can only be accomplished by an anastomosis between the intact portion of the esophagus above the stricture and the stomach, which has been transplanted into the chest, or into the neck.

An esophagogastric anastomosis can be performed after a resection of the stenosed part of the esophagus and cardia, or without resection. The respective advantages and disadvantages of both methods are discussed.

As regards the location of the stricture the following approaches are considered from the technical point of view: (1) In stenoses of the lower fourth of the esophagus left thoracotomy is used. (2) In stenoses of the middle half either a left thoracotomy, particularly in strictures extending behind and above the arch of the aorta, or a right thoracotomy. (3) In stenoses of the upper fourth of the esophagus reconstruction of continuity is possible by high intracervical anastomosis after subtotal resection of the esophagus by the method of Sweet or of Garlock.

In two patients with stricture involving the middle half of the esophagus, palliative operation without resection of the esophagus was performed through a right thoracotomy approach after mobilization of the stomach through the abdomen.

In two other patients with stenosis of the entire thoracic esophagus; intracervical esophagogastrostomy without resection of the esophagus was performed by the retrovascular, intracervical route. This new operative method is described from the anatomical standpoint as well as from technical point of view.

Very good results were obtained in all four patients.

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AN ARTIFICIAL INTIMA FOR PERFUSION APPARATUSES

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IN SUCH a perfusion apparatus as the artificial heart the circulating blood is passing a number of glass and rubber tubes. The inside of these tubes is not as smooth as the intima of arteries or veins.

The perfusion of blood for some hours will therefore cause: (1) slight hemolysis, (2) some fibrin formation, and (3) tendency of foaming.

It has been shown that the fibrin formation and foaming can be avoided by using heavy doses of heparin. As much as 250 mg. of heparin per 1,000 ml. blood is needed for a three hours' perfusion. In intrathoracic operations, however, especially when a sternum splitting approach is used, this heavy heparin dose has been difficult to neutralize by protamine, resulting in a considerable risk of postoperative hemorrhage.

It has, therefore, been found of great value to produce an artificial intima for the circulating blood mainly to delay the clotting of blood. A smaller dose of heparin can then be used and at the end of the perfusion the surplus of heparin can more safely be neutralized by adding protamine to the blood.

In order to produce an artificial intima four different methods have been tried before the coating with Siloxan UHB 300 was chosen.

1. The water-repellent effect of paraffin wax was first tried to delay the clotting of blood in transfusion apparatuses. In the pump of the perfusion apparatus, however, where the rubber tubes are rhythmically constricted by compressed air, the paraffin was found to come off from the walls giving rise to embolism. Even though the blood was filtered before entering the artery of the perfused animal, the risk of embolism made it impossible to use the paraffin wax.

2. Polyvinylchloride has also been used for the coating of tubes. But when two surfaces coated with polyvinylchloride come into contact with each other, parts of the membrane tend to come off giving rise to embolism. The membrane of polyvinylchloride is not more adherent to the wall of the tubes than if a rift is produced, the blood may dissect away the membrane with the danger of embolism. For that reason the polyvinylchloride cannot be used as an artificial intima in the previously mentioned perfusion apparatus.

3. Recently certain plastics, the silicones, have been developed and found to possess water-repellent properties. Through the reaction of methylchlorosilane with the hydroxyl groups of adsorbed water on a surface, a very thin film of methylpolysiloxane is produced, resulting in a very low surface tension. Thus, a very high contact angle of that surface to liquid water is obtained. Water leaves the surface dry and stands in small droplets with a high contact angle.

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The same reaction is found to occur with cotton, wood, wool, silk, glass, rubber, and many other materials. Due to the humidity of the surrounding air, a film of water up to 100 molecules thick is found on the surface of glass which has stood at ordinary room conditions. The methylchlorosilanes appear to react with this strongly bound water film to liberate hydrogen chloride and attach methyl-bearing silicon atoms to the surface, thereby rendering the surface water repellent. The important point is that the silicon atoms appear to be chemically bound to the substrate, probably through oxygen. Once attached, the water-repellent film becomes a part of the object or the substance so treated and remains effective until abraded off (Rochow, 1947).

The organosilicon polymeric substances have a high thermal stability and insulating properties and are widely used in electric industry to produce a permanent water-repellent film maintaining a high surface resistance even when water has condensed on the surface. In 1946, Jaques and co-workers described the valuable properties in delaying the clotting of blood by one of these silicon compounds, General Electric Dri-Film No. 9987 (methyl-chlorosilane). The important point in the method of preparation was, however, to neutralize the liberated hydrochloric acid before the blood came in contact with the surface. The method described by Jaques and associates was, therefore, very time consuming and performed as follows:

All glassware and rubber tubes were carefully cleaned and dried before use.

1. Then methyl-chloro-silane (General Electric Dri-Film No. 9987) was applied in liquid form by pouring it into or through the glassware and rubber tubes used. The methyl-chloro-silane need only to come in contact with the object for a few seconds and the excess was poured off.
2. The object was then rinsed thoroughly with distilled water. The silicon is formed by hydrolysis and fixed to the material.

$$(CH_3)_3Si\,Cl + H_2O = (CH_3)_3Si\,OH + HCl$$

3. The hydrochloric acid liberated was removed by rinsing with very dilute ammonia water.

$$NH_4OH + HCl = NH_4Cl + H_2O$$

4. Then followed a copious washing with distilled water, and the articles were dried in hot air. This procedure gave a film much heavier than an unimolecular film. A fresh application of the silicon was made each time the glassware, etc., were used. The surface was improved with the second and third coatings. For aseptic use, the prepared objects were placed in boiling distilled water for two minutes.

We have used General Electric Dri-Film No. 9987 for preparation of a perfusion apparatus in brain perfusions in dogs. An effective water-repellent surface was obtained in the tubes. It was then possible to decrease the heparin doses to about 100 mg. heparin per 1,000 ml. blood, without clotting, fibrin formation, or foaming. One and one-half hours' brain perfusion did not cause any change of the blood due to the silicon. Nor was any change in the blood chlorides found, indicating that the washing had been carefully performed.

The rubber tubes which had been rhythmically constricted for three hours still had the same water-repellent surface. But the method was too time consuming for practical use, at any rate for a complicated perfusion apparatus.

In cooperation with the Uddeholm Company, Sweden, we have, therefore, worked out a method of coating tubes and glassware with silanoles without the roundabout way over methyl-chloro-silane. This simplification has made it possible to use the silicon as well in a more complicated perfusion apparatus with the same water-repellent effect.

By hydrolysis of methylethoxysilanes and condensation of these produces in appropriate molproportions siloxans are obtained as viscous liquids. This product is produced by the Uddeholm Company, Uddeholm, Sweden, under the registered trade-mark of Siloxan UHB 300.

METHOD

When the tubes and glassware are thoroughly cleaned and dried the Siloxan UHB 300 is poured through the tubes once. A contact with the object for a few seconds is enough. The objects are then kept in an autoclave at 120° C. for one hour. The tubes are placed in such a position that the surplus of Siloxan can run off. Afterward, it is necessary to wash all tubes with sterile saline solution before the perfusion of blood is performed. Thus, the remaining surplus of Siloxan is washed away at the same time as the condensation water in the tubes is removed. Otherwise this water will cause hemolysis. This preparation method has proved to be the best in coating a number of tubes in a more complicated perfusion apparatus. The machine can be coated when put together.

If an isolated part, as a syringe or needle, is coated, Siloxan is first forced through the object, which then is sterilized in an autoclave or boiled in distilled water for five minutes. After washing in saline solution the syringe is ready for use with blood.

This method of coating with Siloxan UHB 300 is now being used before all perfusion experiments. Extensive blood analyses have shown no change due to the Siloxan.

The advantages of the method:

Using Siloxan UHB 300, a water-repellent surface is obtained in glassware and tubes with the following result:

1. The friction is diminished.
2. The clotting is delayed, permitting a decrease of the heparin dose with 60 per cent. For three hours' circulation in the perfusion apparatus 100 mg. heparin per 1,000 ml. blood is sufficient. It has, therefore, been possible to use comparatively more protamine, 100 mg. (10 ml.) neutralizing 50 mg. heparin. The risk of hemorrhage in intrathoracic operations is then on the whole eliminated.
3. The fibrin formation is decreased.
4. The risk of foaming is diminished.

The artificial intima produced by Siloxan UHB 300 will, furthermore, render the apparatus easy to clean after use. After rhythmical constriction of the tubes for three hours, the walls are still as water repellent as after the coating. The same coating has been used for three different perfusions one week apart. At the mechanical cleaning of the apparatus, however, some part may lose the water-repellent effect. It is, therefore, advisable to perform a new coating before each perfusion. We have also found it advantangeous to use Siloxan for coating of apparatuses for blood transfusions and intravenous administration, needles, cannulas, and syringes.

SUMMARY

A simple method is described for coating of glassware and rubber tubes with Siloxan UHB 300. An effective water-repellent surface is produced acting as an artificial intima diminishing the friction, the foaming, the fibrin formation, and delaying the clotting of blood so that a comparatively smaller heparin dose can be used.

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COEXISTING BRONCHIOGENIC CARCINOMA AND COCCIDIOIDOMYCOSIS

REPORT OF A CASE

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EXPLORATORY thoracotomy in the management of suspicious intrathoracic lesions in which a positive diagnosis is not obtainable, although not universally accepted, is being performed with increasing frequency throughout the United States. It is only reasonable to expect that in our ambitious quest to conquer bronchiogenic carcinoma unusual lesions will be discovered at exploratory operations in increasing numbers. It has been recently pointed out by Brewer and Dolley that, in cases in which the lesion is found to be a benign one, the ideal treatment of most of these lesions is resection.

It has only been since the close of World War II that coccidioidomycosis has become a nationwide disease and must therefore be considered in the differential diagnosis of most chronic pulmonary lesions. As yet, the indications for surgical treatment of the pulmonary lesions of coccidioidomycosis have been limited, and reported series of cases have been few.

The following case is the first of its kind that we have seen. A search of the literature reveals that Churchill, in 1947, reported two cases of malignant lymphoma of the lung associated with coccidioidomycosis and stated that by personal communication Maier had reported a similar case. Other than these related cases our review of the literature has failed to reveal a reported case of primary bronchiogenic carcinoma associated with coccidioidomycosis in the same lung. Not having access to foreign and some American literature, except by title and published abstracts, our review is not complete and the author welcomes correction if a similar case has been reported.

CASE REPORT

J.W.B., a 53-year-old white male brush salesman, entered the hospital upon advice of a private physician. During a mass x-ray campaign in March, 1949, of the local tuberculosis association a 35-mm. photofluorographic film was made of his chest. Upon the basis of findings in the film he was recalled and given a tuberculin skin test which was negative. He was then advised to see a private physician for investigation of a suspicious lesion of the left chest. He neglected to report to a doctor until September, 1949. History revealed that the patient had had a chronic cough productive of one-fourth cup of thick yellow sputum for several years. In February, 1949, the patient contracted an upper respiratory infection characterized by marked aggravation of the cough and an increase in the amount of sputum to one cup per day. He did not consult a physician about the "cold" and symptoms spontaneously subsided after three months. Since that time, however, he had felt "run down" and fatigued and had not been able to work at his occupation more than two to three hours daily. He denied hemoptysis, night sweats, weight loss, and all other symptoms.

From the Surgical Service of the United States Naval Hospital.

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Past History.—The past history revealed that the patient had been subjected to the usual childhood diseases and influenza in 1918. He was diagnosed as having a peptic ulcer in 1935, which responded to a short period of rest and diet. He had intermittently consulted a physician for several years for "colitis" characterized by infrequent diarrhea and excessive mucus in the stools.

He had had mild hypertension (140/100) for four years prior to admission and for four years had been subject to typical anginal pain brought on by exertion and relieved by rest.

The patient was born in Illinois where he lived for 20 years, following which he moved to Florida where he resided for 15 years. For the five years preceding admission, he had lived in Southern California in Imperial Beach for two years and Chula Vista for three years. He had never been in the San Joaquin Valley. Neither had he been a resident of any of the southwestern states.

Family History.—The family history was noncontributory.

Physical Examination.—Physical examination revealed a well-nourished, well-developed, slightly obese, white man, who did not appear acutely or chronically ill. The blood pressure was 140/100, the pulse 88, and the respiration 22. The temperature was 99° F. Except for fine râles in the left lower lobe posteriorly which cleared on coughing, the physical examination was negative.

Laboratory studies showed a normal urine. The hemoglobin was 17 grams per 100 c.c. and the white cell count was 4,750 with normal differential distribution. Three examinations of the sputum for tubercle bacilli were negative. Tuberculin skin test in a dilution of 1:1000 produced a 20 by 20 mm. erythema. Serologic titer for coccidioidomycosis by complement fixation was not done preoperatively. Blood Kahn was negative. Electrocardiogram revealed marked slowing of the interventricular conduction rate.

X-ray studies of the chest were done. Stereoscopic views of the chest revealed a peripheral mass lying against the lateral chest wall measuring 5 by 8 cm. The impression of the radiologist was (1) encapsulated fluid, (2) possible tumor of the lung or chest wall. Laminagraphs of this area were done which revealed the center of the mass to be at a depth of 12 cm. from the back and indicated that the mass was about 5 cm. in thickness. A diagnostic pneumothorax revealed the lung to be adherent to the chest wall at the site of the mass, and the radiologist was still unable to determine if the mass lay within the lung field. In addition, a 2-cm. circumscribed area of increased density was seen in the apex of the upper lobe, which, prior to the pneumothorax had occupied a position under the first rib and clavicle and was present in previous films in retrospect. Impression at this time was "tuberculosis, however, lung tumor cannot be ruled out."

Bronchoscopy revealed a small eroded area on the medial wall of the left main bronchus 1 cm. below the carina. Biopsy from this area was negative. Smears from aspirated material taken at bronchoscopy and repeated smears from sputum were studied by Papanicolaou's method were negative for evidence of malignancy. Bronchoscopy prior to surgery failed to reveal the previously described ulceration.

On Oct. 13, 1949, *exploratory thoracotomy was performed.* The left pleural cavity was opened through the sixth rib bed. There was a dense mass in the posterior apical segment of the upper lobe which was densely adherent to the chest wall. Closely adjacent to this in the apical portion of the lobe was a 2-cm. nodule which was very firm. There were pea-sized nodules distributed throughout the lower lobe. Upon freeing the mass from the chest wall, a 5 by 5 cm. thick-walled cavity filled with a caseous appearing material was entered. It was felt at that time that a tuberculous process had been encountered and a lobectomy was done. The vessels to the upper lobe and the superior pulmonary vein were triply ligated with silk ligatures and divided. The bronchus was severed and closed with simple interrupted sutures of fine silk. The chest wall was closed in individual layers with interrupted cotton sutures. Intercostal tubes were placed in the fourth interspace in the anterior axillary line and in the ninth interspace in the posterior axillary line and connected to a water-seal bottle.

Frozen section of the removed specimen during the operative procedure was reported as epidermoid carcinoma. This section was taken from the solid tumor mass, the pathologist assuming that the cavitation was necrotic tumor. On the basis of the report it was deemed that the lesion was inoperable because of the chest wall invasion over a wide area. Also at the time the report was received, the operating time had exceeded three and one-half hours and the condition of the patient would not have permitted further resection.

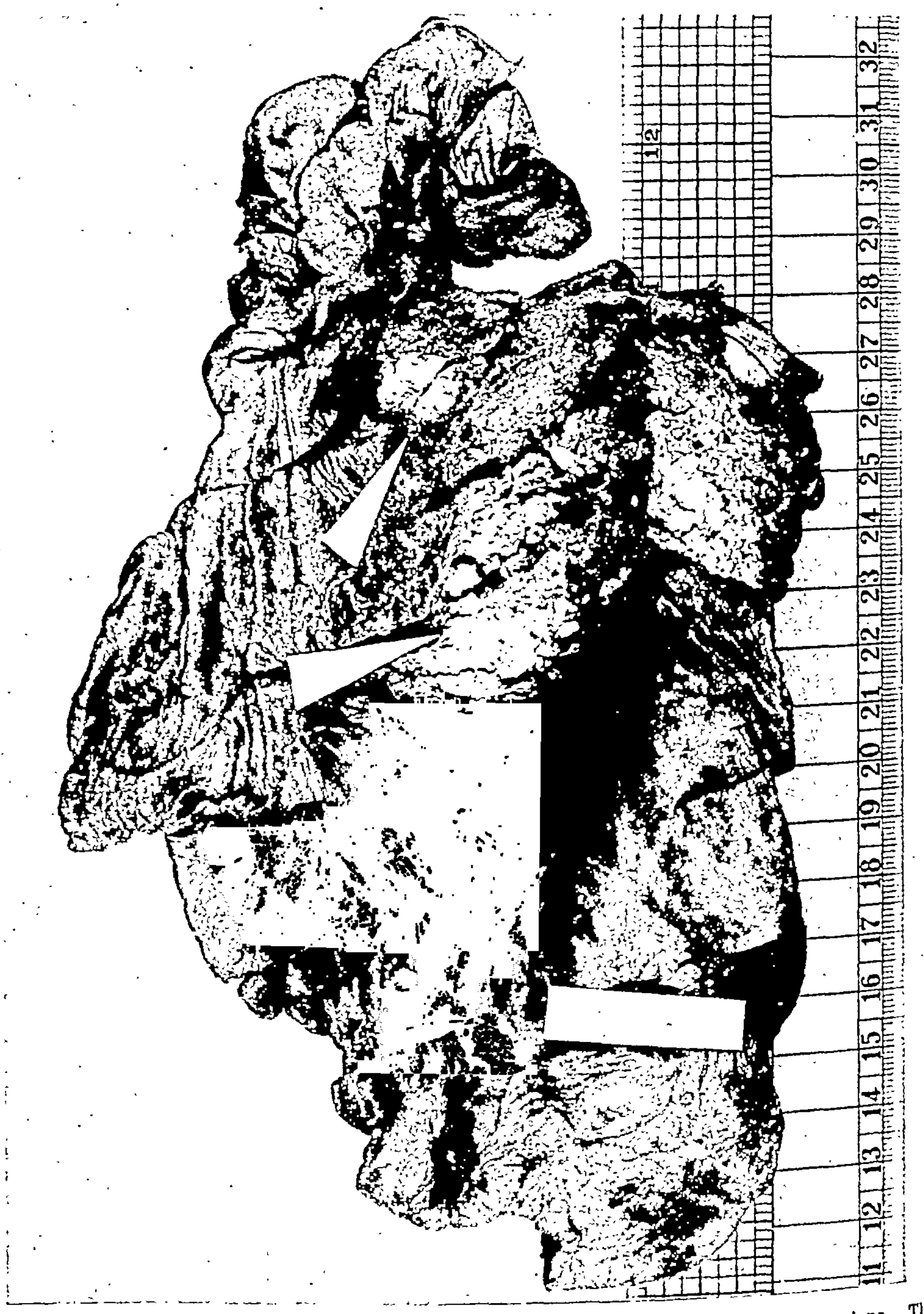

Fig. 1.—The formalin fixed upper lobe showing the relation of the two lesions. The rounded discrete mass lying superiorly is the epidermoid carcinoma. The larger mass with cavitation is the lesion found to contain *Coccidioides immitis*.

The patient's convalescence was uneventful, and the tubes were removed on the third postoperative day.

Pathologic Report.—Gross examination of the specimen revealed it to consist of the left upper lobe of the lung measuring 16 by 9 by 6 cm. The pleural surface was roughened on its lateral aspect. The lung on palpation revealed two distinct tumors, one located near the periphery in the mid-portion of the lung, and the other located superiorly to and deeper *in the lung parenchyma than previously described. Accompanying the specimen were two* lymph nodes which were peribronchial nodes of the left upper lobe. The nodes appeared to be grossly involved with neoplastic tissue. On sectioning the lung a firm tumor mass 2 cm. in diameter was located in the apical segment of the lobe. This mass was grayish-white, discrete, but not encapsulated. A second mass lying lateral and inferior to the first mass was found to measure 5 cm. in all diameters. The mass was filled with white, cheesy tissue, and the wall of the mass was granulatory in character. It was encapsulated and no tumor was seen grossly. The remainder of the lung parenchyma was not remarkable.

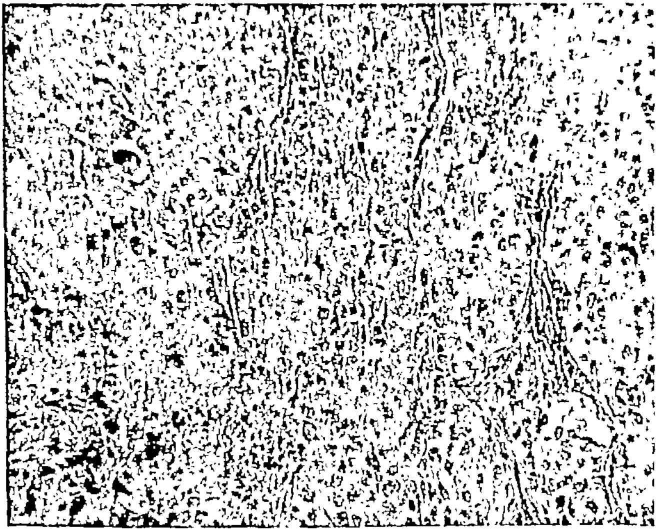

Fig. 2.—Photomicrograph of a section from the carcinoma which is a squamous-cell or epidermoid carcinoma.

Microscopic examination of the lymph node revealed sheets of anaplastic epidermoid cells completely replacing the normal architecture.

Sections from the solid tumor mass from the lung revealed an anaplastic epidermoid carcinoma with many mitoses, hyperchromatic bizarre nuclear patterns, and complete loss of tissue architecture. A segment of bronchiolar epithelium revealed a marked epidermidization of the lining epithelium.

Sections of the peripheral mass showed it to consist of a rather dense fibrous wall lined by necrotizing granulation tissue. The center of the mass was composed of necrotic tissue. Double-contoured spherical spores measuring from ten to fifty micra, characteristic of *Coccidioides immitis*, were found distributed in the necrotic tissue and in the wall of the lesion.

The diagnosis was: (1) Epidermoid carcinoma of lung with metastasis to regional lymph nodes. (2) Coccidioidomycosis of the lung.

After pathologic examination had been complete it was apparent that two separate lesions were present and that the carcinoma was localized and was grossly operable. Complete mediastinal lymph node resection had not been done at the time of surgery. It was decided, therefore, that reoperation with complete pneumonectomy and excision of lymph nodes was indicated.

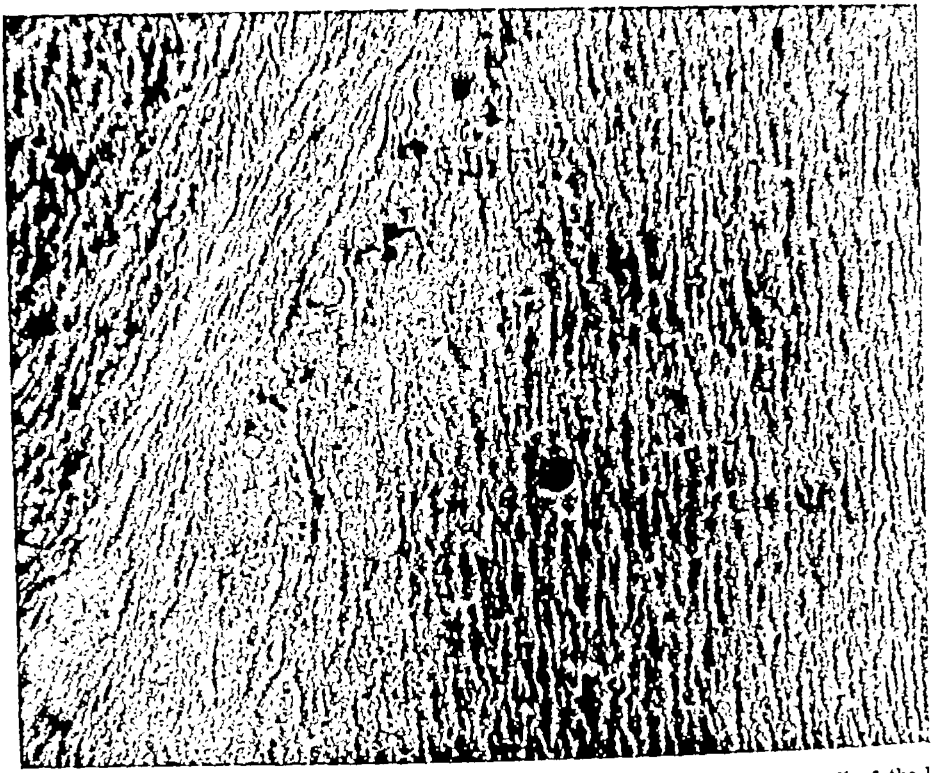

Fig. 3.—Photomicrograph of the cavitary lesion. The section is through the wall of the lesion. Three spores of *C. imitis* are clearly visible in this section.

On Oct. 31, 1949, the patient was operated upon again. The previous incision was reopened. The left lower lobe was mobilized. The pericardium was opened and the common left pulmonary vein was triply ligated with heavy silk and divided. The pulmonary artery was mobilized to its origin and similarly ligated. The left main bronchus was amputated within one centimeter of the carina and closed with simple interrupted sutures of 0 silk. All accessible hilar and mediastinal lymph nodes were resected. No evidence of tumor was seen grossly in the specimens. The pleural cavity was closed, and the chest wall was repaired as before. Pathologic examination of the removed tissue revealed no evidence of carcinoma. All lymph nodes were negative. A small 1 by 1 cm. area of granulomatous tissue was found in the pulmonary ligament which proved to be a pleural lesion of coccidioidomycosis.

The patient's postoperative course was uneventful until the fourth postoperative day, when he suddenly began coughing up blood-stained material and rapidly went into profound circulatory collapse. Examination revealed a tension pneumothorax on the operated side with a marked shift of the mediastinum to the right. It was apparent that a bronchopleural fistula had developed. An intercostal tube was inserted by trochar and connected to a water-seal bottle. Intratracheal aspiration was repeatedly done and bronchoscopy was employed to remove material aspirated from the pleural cavity through the opened bronchial stump. Evidence of a rather marked paradoxical mediastinal motion was present and pulmonary edema developed in the right lung. The patient was digitalized with slight improvement. The patient's course from this point was progressively downhill, and he expired from cardiac failure on the seventh postoperative day.

Autopsy revealed besides the disrupted bronchial stump and an early empyema that the right lung was extremely emphysematous. Also a grade 4 coronary arteriosclerosis was present. There were small nodules in the right lung which proved to be focal lesions of coccidioidomycosis. No evidence of residual or metastatic carcinoma could be detected.

A diagnosis of active coccidioidomycosis could have been made by employing complement fixation tests; however, if it had been made preoperatively the carcinoma would have been neglected until a much later date.

Although the operative procedure was performed because carcinoma could not be ruled out, we feel that the tumor in this case was an incidental finding. Whether pneumonectomy was indicated in this case remains a question. The author feels that since metastatic tumor was found in the peribronchial lymph nodes at the first operation, reoperation was imperative.

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RESPIRATORY AND CIRCULATORY STUDIES AFTER PNEUMONECTOMY IN CHILDHOOD

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ALTHOUGH seventeen years have elapsed since the first successful one-stage pneumonectomy was performed, relatively little detailed information is available regarding respiratory and circulatory function of individuals in whom a lung has been removed. This dearth of knowledge is particularly striking in pneumonectomized children.

In 1937, Bremer[1] investigated the histologic changes in the remaining lung occurring after experimental pneumonectomy. In growing cats what was considered to be a true hyperplasia of the parenchyma was found, whereas in adult animals simple alveolar distention took place.

Longacre, Carter, and Quill[2] determined lung volume, response to exercise, and tolerance to low oxygen in two groups of dogs following pneumonectomy. The adult animals showed marked deficiency in respiratory reserve. Although their functional residual air volumes were abnormally large to such extent that they equalled prepneumonectomy values, they could perform moderate exercise adequately. Operated puppies, on the other hand, did as well as their unoperated litter mates on both moderate and strenuous effort even though the remaining lung filled the entire thorax.

In a later communication Longacre and Johansmann[3] reported experimental studies four years after pneumonectomy which represents about one-half the life span of the normal dog. In the adult animals fragmentation of alveoli and loss of elastic tissue were found, while the dogs operated on as puppies demonstrated only a slight amount of alveolar membrane rupture. The physiologic performance of the latter group was nearly normal whereas the former showed deficiencies on all tests.

There have been a number of investigations on adult human beings following pneumonectomy but only two on children, reported by Lester and associates.[4a] Three children aged 9, 12, and 14 years who had left pneumonectomies were studied. All three cases were complicated by postoperative empyema. When the study was made, one to three years after operation, all were in good clinical condition. They performed exhausting exercise without changes in blood gas composition other than those expected in normal individuals. The lung volumes were larger than expected for one normal lung but not as large as predicted for two. In none of them did the lung fill the opposite hemithorax completely. The

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patient with the most marked herniation had poorer function than the other two. The authors concluded that overdistention of the lung following pneumonectomy was undesirable and that steps should be taken to prevent displacement of the mediastinum.

In a second paper[4b] the same three patients were studied five to six and one-half years after operation in addition to a 20-year-old girl who had a left pneumonectomy completed at the age of 16 years. Two patients showed improved adaptation and good performance. The remaining two showed a drop in arterial oxygen saturation after exhausting exercise. The latter cases also had reduced breathing reserve and increased ratio of residual air to total capacity. In one of these cases, the 20-year-old girl, a thoracoplasty had been performed in an attempt to relieve distention with some subjective but no objective improvement.

The preceding studies include only patients with postoperative empyema in whom the mediastinum may be more rigid than normally is the case. One of the patients was 16 years old at the time of operation and therefore past her maximal growth period. It seemed, therefore, desirable to us to study a larger series of children on whom pneumonectomy uncomplicated by empyema had been performed in early childhood.

CLINICAL MATERIAL

Of the twenty-two children who have had a pneumonectomy at Barnes Hospital, ten have been studied. Of the remaining twelve, five died in the immediate postoperative period, one survived eight years but met an accidental death, two were too young for satisfactory evaluation, and four cannot be located.

In the group examined, operation was performed because of unilateral bronchiectasis or abscess in seven and actinomycosis, granuloma of unknown etiology, and lipoid pneumonia in the remainder. In all but one of these cases there is no disease in the remaining lung. The group includes seven girls and three boys whose ages at operation ranged from 3 to 14 years. At the time of study eight months to thirteen years had elapsed since operation which was performed on the right in four and on the left in six. There was only one postoperative empyema and no bronchopleural fistulas. All but three pneumonectomies were done by individual ligation technique.

At the time of study all but the patient with residual disease were leading normal lives. One girl (J. W.) now 21 years old is a champion gymnast and a 19-year-old boy (S. H.) is doing construction work 4,000 to 5,000 feet above sea level. None of the patients had any significant scoliosis or other cosmetic deformity. Age at operation, sex, height, weight, body surface, and diagnosis are given in Table I.

METHODS

The patients were examined early in the morning, fasting or after a light breakfast. Vital capacity and its subdivisions were determined in the supine position with a standard metabolism machine filled with oxygen. The complemental air values include tidal air as suggested by Christie. A wait of at least twenty minutes was allowed after these tests in order to restore normal gas relationships in the lung. Residual air was then measured with the patient supine by the closed method of Cournand and associates,[5] modified by placing an additional three-way valve between the main three-way valve and the spirometer circuit. This renders it unnecessary for the patient to hold his breath at the end of the alveolar sampling. The technique involved seven minutes of oxygen breathing during which time the expired air was collected in a spirometer. At the end of seven minutes an alveolar sample was obtained. The nitrogen percentage of this and of the spirometer content was determined in the Van Slyke-Neill apparatus according to the method described by Peters and Van Slyke[6] with minor modifications. Duplicate determinations checked within .03 volumes per cent.

Considerable difficulty was encountered in residual air determinations on young children and the results cannot be expected to check as well as in adults. However, alveolar nitrogen values in duplicate tests checked adequately in all instances. The difference between duplicate values of the residual air determinations was less than 12 per cent in five subjects. In the remaining five it varied from 16 to 34 per cent. Only in patients with large residual air compartments were the differences between duplicate determinations great.

To measure maximum breathing capacity, the patient was encouraged to breathe as deeply and as rapidly as possible in the erect position for two periods of fifteen seconds and two periods of thirty seconds. The expired air was collected in a 350-liter spirometer by means of two one-way flutter valves. The diameter of the connecting tubing was one and one-half inches. The highest value of the four obtained, expressed as liters per minute, corrected to prevailing barometric pressure at 37° C., and saturated with water vapor, was used.

Following another twenty-minute rest period a femoral arterial blood sample was withdrawn in a lightly lubricated syringe the dead space of which was filled with undiluted heparin. The patient then performed a standard exercise which consisted of walking on a treadmill at a five degree grade for seven minutes at a speed of either 2.5 or 3.2 miles per hour, depending on the size of the subject. During each minute of exercise and at three, five, and ten minute intervals afterward pulse and respiratory rates were recorded. Immediately upon completion of exercise another arterial blood sample was withdrawn. Part of each blood sample was centrifuged under oil and the plasma collected over mercury for carbon dioxide content and pH determinations in duplicate. The former was done according to the 0.2 c.c. method as described by Peters and Van Slyke,[6] the latter with the method of Hastings and Sendroy[7] using bicolor standards. The remaining blood was used for the determination in duplicate of oxygen content and capacity in the Van Slyke-Neill apparatus. All gasometric analyses checked within 0.12 volumes per cent. The carbon dioxide tension was computed from the pH and carbon dioxide content by means of the Henderson-Hasselbalch equation using the line chart of Peters and Van Slyke.[6]

Finally, inspiratory and expiratory posterior-anterior x-ray films of the chest were taken as well as a lateral film of the nonoperated side in most instances. These were reviewed by Dr. William B. Seaman of the Mallinckrodt Institute of Radiology who rated each case from one to four plus for diaphragmatic motion, mediastinal motion, and degree of herniation of the lung into the opposite hemithorax. An estimate was also made of the size of the thoracic cage on the operated side expressed as a percentage of the size of the nonoperated side in the inspiratory position.

RESULTS

The results of these studies are shown in Tables I to VI. The patients listed above the rule are children with the left lung remaining, those below, the right. G. K. will be discussed separately since she was the only child in whom there was residual disease.

TABLE I. BODY CHARACTERISTICS AND DIAGNOSES OF CASES STUDIED

SUBJECT	SEX	HEIGHT IN CM.	WEIGHT IN KG.	SURFACE AREA IN M²	AGE AT OPERATION (YEARS)	NUMBER OF YEARS SINCE OPERATION	DIAGNOSIS
				Left Lung Remaining			
M.P.*	F	167.8	51.8	1.57	3	12	Infected cystic disease
J.L.*	M	170.0	54.5	1.68	12	4	Chronic lung abscess with bronchopleural fistula
D.T.	F	165.0	61.7	1.67	14	3	Actinomycosis
G.K.†	F	147.3	42.2	1.30	10	1	Granuloma of lung
				Right Lung Remaining			
J.R.*	M	127.5	26.8	0.97	5	2	Lung abscess with bronchiectasis
J.B.‡	F	140.0	31.8	1.12	6	6	Bronchiectasis due to aspirated foreign body
G.S.	F	144.0	34.0	1.05	12	8/12	Granuloma of unknown etiology
B.S.	F	151.0	37.2	1.26	3	10	Bronchiectasis due to aspirated foreign body
S.H.	M	184.0	68.1	1.88	13	6	Bronchiectasis due to aspirated foreign body
J.W.	F	162.5	55.0	1.58	8	13	Bronchiectasis due to aspirated foreign body

*Preoperative empyema.
†Residual disease in remaining lung.
‡Postoperative empyema but no bronchopleural fistula.

The oxygen saturation before and after exercise (Table II) was within normal range in all subjects, increasing 1 to 4 per cent in all but M. P. after effort. An oxygen capacity rise averaging 0.73 volumes per cent similar to that found in normal subjects was also noted. The plasma carbon dioxide content and pH were within the normal range before and after exercise as was the carbon dioxide tension except in the case of G. S. This last value is undoubtedly due to a technical error. The respiratory rates with exercise (Table III) were higher than the normal figures given by Robinson.[9] At the end of

TABLE II. ARTERIAL BLOOD STUDIES BEFORE AND AFTER EXERCISE

	OXYGEN SATURATION %		OXYGEN CAPACITY VOL. %		PLASMA CO_2 CONTENT MEQ./L		PLASMA PH		ARTERIAL CO_2 TENSION MM. HG	
SUBJECT	BEFORE EXERCISE	AFTER EXERCISE	BEFORE EXERCISE	AFTER EXERCISE	BEFORE EXERCISE	AFTER EXERCISE	BEFORE EXERCISE	AFTER EXERCISE	BEFORE EXERCISE	AFTER EXERCISE
				Left Lung Remaining						
M.P.	95.38	95.10	17.30	18.28	24.30	18.75	7.50	7.35	32.9	36.1
J.L.	95.50	96.87	20.20	21.12	24.44	22.38	7.47	7.47	35.0	32.8
D.T.	96.00	96.97	17.75	19.10	24.54	19.45	7.50	7.40	33.0	33.0
G.K.*	90.18	81.32	22.01	22.90	26.20	24.10	7.50	7.35	35.0	46.0
				Right Lung Remaining						
J.R.	93.98		17.95		22.42		7.40		35.7	
J.B.	94.60	95.35	18.43	18.97	24.63	24.11	7.47	7.47	35.2	35.0
G.S.	95.28	99.25	18.65	19.41	22.42	25.78†	7.43	7.38	35.2	51.9
B.S.	96.83	97.83	16.63	16.03	20.77	20.45	7.45	7.40	31.0	35.1
S.H.	97.08	99.68	22.60	23.07	24.42	23.98	7.55	7.50	29.3	32.0
J.W.	94.00	96.52	17.35	18.26	18.85	22.02	7.35	7.37	35.8	39.1

*Residual disease in remaining lung.
†Probable technical error.

TABLE III. PULSE AND RESPIRATORY RATES DURING AND AFTER EXERCISE

SUBJECT	PULSE		RESPIRATIONS	
	MAXIMUM RATE WITH EXERCISE	RATE 10 MINUTES AFTER EXERCISE	MAXIMUM RATE WITH EXERCISE	RATE 10 MINUTES AFTER EXERCISE
	Left Lung Remaining			
M.P.	148	102	32	20
J.L.	136	60	32	20
D.T.	192	92	44	20
G.K.*	140	124	84	42
	Right Lung Remaining			
J.R.	112	96	40	22
J.B.	132	92	40	20
G.S.	156	118	30	20
B.S.	176	104	36	16
S.H.	140	76	28	17
J.W.	148	84	36	16

*Residual disease in remaining lung—tolerated only two minutes of exercise.

a ten-minute recovery period, however, the rate was 22 or below in all subjects. The pulse rate in the same interval had returned to 100 or below except in one individual studied only eight months after operation. Those in better physical condition such as S. H., J. W., and J. L. had the slowest pulse at the end of the ten-minute rest period.

Table IV lists the absolute values found for each of the subdivisions of the lung volume, the maximum breathing capacity, and the per cent of alveolar nitrogen after seven minutes of oxygen breathing. To evaluate these results some standard of reference is necessary. The values for comparable normals reported in the literature by different investigators vary considerably. The prediction formulas of Baldwin and associates for vital capacity and maximum breathing capacity[8] are satisfactory in older children and adults but are not derived from or useful for predicting values in younger children. Thus figures obtained by using these formulas are much larger than those found by Robinson[9] in normal boys and by Wilson and Edwards[10] in children of both sexes.

TABLE IV. TOTAL LUNG VOLUME—ITS SUBDIVISIONS AND MAXIMUM BREATHING CAPACITY*

SUBJECT	TIDAL VOLUME (C.C.)	COMPLEMENTAL VOLUME (C.C.)	RESERVE VOLUME (C.C.)	VITAL CAPACITY (C.C.)	RESIDUAL VOLUME (C.C.)	TOTAL VOLUME (C.C.)	$\frac{\text{RESIDUAL}}{\text{TOTAL}} \times 100$	% ALVEOLAR N_2 AFTER 7 MIN. O_2 BREATHING	MAXIMUM BREATHING CAPACITY (L/MIN.)
				Left Lung Remaining					
M.P.	313	1585	501	2035	3271	5357	61.0	6.41	45.3
J.L.	628	1909	602	2510	1124	3635	30.8	1.05	63.5
D.T.	289	1417	210	1680	650	2277	28.6	1.27	48.9
G.K.†	236	483	129	559	747	1359	54.6	1.86	30.9
				Right Lung Remaining					
J.R.		1063	330	1118					46.0
J.B.	319	904	186	1116	1038	2128	48.8	1.32	35.2
G.S.	369	1055	190	1212	2706	3900	69.1	3.86	36.4
B.S.	310	1500	310	1810	1060	2870	37.0	1.08	54.1
S.H.	536	2678	1102	3640	1241	5025	24.7	1.90	92.5
J.W.	479	1915	718	2660	997	3625	27.4	1.45	52.0

*All volumes are at barometric pressure 37° C. and saturated with water vapor.
†Residual disease in remaining lung.

TABLE V. COMPARISON OF VITAL CAPACITY, TOTAL CAPACITY, AND MAXIMUM BREATHING CAPACITY EXPRESSED IN PER CENT OF VARIOUS STANDARDS FOR TWO NORMAL LUNGS

SUBJECT	AGE AT STUDY (YEARS)	SEX	VITAL CAPACITY*					TOTAL CAPACITY*				MAXIMUM BREATHING* CAPACITY	
			I	II	III	IV	V	I	II	III	IV	I	II
			Left Lung Remaining (Normal—45 per cent of total)										
M.P.	15	F	54	60	55	75	71	113	127	114	121	41	45
J.L.	10	M	54		51	52		63		58	57	51	61
D.T.	17	F	51		45	53		55		49	51	46	
G.K.†	10	F	18	30	19		23		57	36		36	30
			Right Lung Remaining (Normal—55 per cent of total)										
J.R.	7	M	33		65		61						
J.B.	12	F	39	59	51		54		90	76		48	52
G.S.	12	F	41	64	55		63		165	140		53	46
B.S.	13	F	57	87	61		79		110	77		66	70
S.H.	19	M	77		73	76		85		77	82	64	
J.W.	21	F	84		72	85		91		78	82	54	

*I. Formulas of Baldwin and associates.[4]
II. Normal values Cournand and associates.[4]
III. Normal values Robinson.[9]
IV. Normal values Hurtado and associates.[11, 12]
V. Normal values Wilson and Edwards.[10]
†Residual disease in remaining lung.

In the only study of normal female subjects (Hurtado and associates[11]) the age range is from 17 to 34 years. The difficulty in comparing our results with normal data is evident in Table V where the values obtained in our subjects are expressed as a percentage of those predicted for two lungs by various authors for normal subjects of similar age and body fluid. As an example, it can be seen that the vital capacity of B. S. ranged from 57 to 79 per cent of normal with different standards.

In all cases the tidal air was greater than would be expected for one lung; and in most, subjects approached the normal value for an intact individual. Complemental air was also greater than predicted. Reserve air was larger than expected for one lung in four; in the remaining six it was less. All of

TABLE VI. RADIOLOGIC EVALUATION OF DIAPHRAGMATIC AND MEDIASTINAL MOTION AND SIZE OF OPERATED HEMITHORAX*

SUBJECT	DEGREE OF DIAPHRAGMATIC MOTION	DEGREE OF MEDIASTINAL MOTION	DEGREE OF HERNIATION INTO THE OPPOSITE HEMITHORAX	OPERATED SIDE AS PER CENT OF THE NONOPERATED
		Left Lung Remaining		
M.P.	2	0	4	80
J.L.	4	1	3	70
D.T.	4	1	1	70
G.K.†	2	1	3	100
		Right Lung Remaining		
J.R.	1	2	2	90
J.B.	2	1	1	40
G.S.	1	0	1	100
B.S.	2	1	4	90
S.H.	3	4	2	100
J.W.	4	4	4	90

*Magnitude of motion rated from 1 to 4 plus.
†Residual disease in remaining lung.

our cases had vital capacity values at least as great as could be predicted for the remaining lung. In some it was markedly greater. The maximum breathing capacity similarly showed values as large as, or up to 10 per cent greater than, that predicted for one lung. As the resistance in our system was higher than in the apparatus used in the control studies with which we are making comparison, the performance on this test might be better than the percentages would indicate.

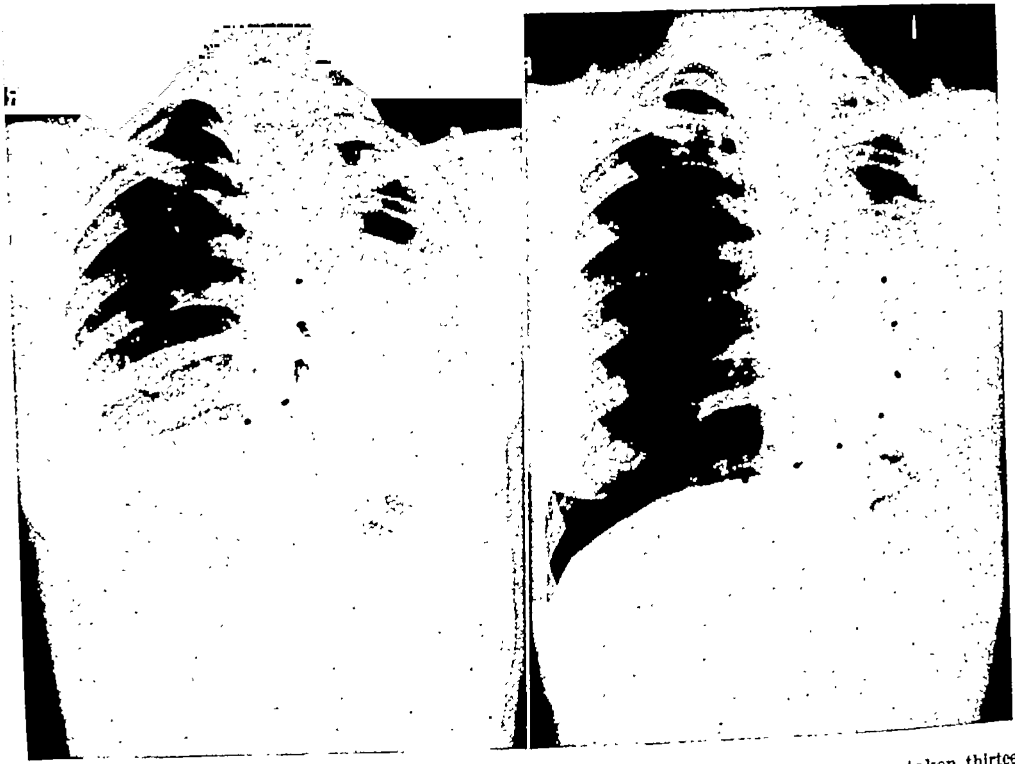

Fig. 1 (J. W.).—Expiratory (left) and inspiratory (right) roentgenograms taken thirteen years after left pneumonectomy. Moderate mediastinal shift and marked herniation of remaining lung into opposite hemithorax. Wide range of mediastinal motion (dotted lines) and diaphragmatic descent (two interspaces) associated with superior physical capacity and normal ratio of residual air to total lung volume (27 per cent).

Evidence of an increase in size of the remaining lung is afforded by values of total lung volume greater in all cases studied than that predicted for a similar normal lung. In three individuals (M. P.,* G. S., and B. S.) the total capacity was even greater than expected in a normal individual with two functioning lungs. In two of these children (M. P. and G. S.) emphysema is suggested by the very high ratio of residual air to total capacity. In the third subject (B. S.) as well as in three others (J. L., J. W., and S. H.) increased total capacity went pari passu with larger than expected vital capacity and in them a hyperplasia of lung tissue may have occurred.

In the two patients with highest residual air volumes high alveolar nitrogen values were encountered after seven minutes of oxygen breathing. Duplicate determinations of these nitrogen concentrations in alveolar air checked satisfactorily. These high values are believed to be evidence of poor ventilation of some portions of the lung and not due to technical errors. In all other patients the alveolar nitrogen concentrations were within normal limits. Of the eight on whom satisfactory values were obtained, four had a ratio of residual air to total capacity below 30 per cent which may be taken as normal for this age group. The other four all had ratios which must be considered above normal.

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*At the time of her operation 12 years ago, so far as was known, she was the first very young child (3 years of age) to have a pneumonectomy. There was some worry that the procedure might interfere with her normal growth and development, but fortunately she appears and acts now like any normal girl of 15 years.

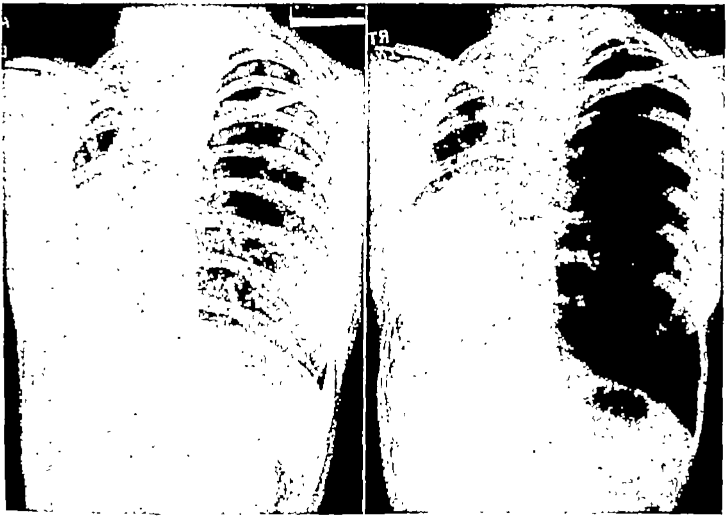

Fig. 2 (M. P.).—Expiratory (left) and inspiratory (right) roentgenograms taken twelve years after right pneumonectomy. Marked herniation of lung and marked mediastinal shift with heart in right thorax. Only moderate diaphragmatic motion (one interspace) and no mediastinal motion on deep inspiration. Residual air compartment 69 per cent of total lung volume.

The condition of the remaining lung, as judged from the x-ray films, correlated well with the functional studies. All patients had herniation of the lung into the opposite hemithorax to a greater or less degree. However, in those patients with evidence of a wide range of mediastinal and diaphragmatic motion the herniation, although large, did not result in a large residual air compartment, and their ventilatory performance was excellent (Fig. 1). As the diaphragmatic and mediastinal mobility was reduced the herniation took place in association with increased residual air. In the two cases with the highest ratio of residual air to total capacity, no mediastinal motion was found (Fig. 2). In other words, the highest residual air percentages were all associated with two plus or less motion of both mediastinum and diaphragm. The two subjects with the largest vital capacities as compared to the predicted values had the greatest mediastinal and diaphragmatic movement.

In six of the ten, the size of the hemithorax on the operated side, as judged by radiography, was essentially the same as that on the unoperated side. The postoperative empyema in J. B. may have resulted in a contraction of ipsilateral hemithorax to 40 per cent of the size of the opposite side. The remaining three patients had slightly reduced ipsilateral hemithoraces; two of these experienced empyema before operation but the other had no pre- or postoperative complications.

Thus far G. K. has not been discussed because of the disease in her remaining lung. She is a pulmonary cripple, and could exercise for only two minutes at the end of which time her arterial oxygen saturation had fallen to 81 per cent and carbon dioxide tension had risen to 46 mm. Hg. Her vital capacity and maximum breathing capacity were less than expected for the remaining lung and her residual air compartment was large. She is the only patient who manifested any abnormalities in blood gas values on exercise.

SUMMARY AND CONCLUSIONS

There is no apparent correlation between age at operation and physiologic performance as determined by the methods used. Except for perhaps the first year, the interval after operation would seem not to influence the result.

In comparing our patients with Cournand's four children studied after pneumonectomy, we find essentially similar vital capacity data. In maximum breathing capacity two of his subjects exceeded the best of our series, but the difference in technique may have made this discrepancy more apparent than real.

We have found a high residual air in one-half of our subjects, but even this finding, together with reduced ventilatory ability, has not prevented any of them from performing moderate exercise for seven minutes in a normal way and without fall in arterial oxygen saturation. Cournand has raised the question whether herniation of the remaining lung into the opposite hemithorax should not be prevented by thoracoplasty or oleothorax. We find, however, that herniation of considerable degree can be associated with low residual air values and excellent vital capacity and maximum breathing capacity if the mobility of diaphragm and mediastinum is maintained at a maximum. One of the most striking and provocative findings from our studies is that the best performance on all tests was found in the two most active patients, the gymnast and the construction worker, each of whom has made a concerted effort to overcome his handicap. This observation suggests the importance of physical training after pneumonectomy and the maintenance of the maximum mobility of diaphragm and mediastinum.

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PERICARDIAL CELOMIC CYSTS AND PERICARDIAL DIVERTICULA

A CONCEPT OF ETIOLOGY AND REPORT OF CASES

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THIN-WALLED cysts of the mediastinum, filled with a clear fluid and lined with mesothelium, constitute a relatively new clinicopathologic entity. The contemporary problem of the origin and significance of these cysts may be said to have arisen in 1934, when Pickhardt[1] first reported the successful removal of a "pleuropericardial cyst" from the mediastinum. Prior to this time, discussion of the etiology of these cysts had been confined to pathologico-anatomic reports which date well back into the past century. Rokitansky[2] in 1854, Cruveilhier[3] in 1849, Hird[4] in 1848, Coën[5] in 1885, and Rohn[6] in 1905, described cysts which they considered to have been formed by herniation of the serosa of the pericardium through the fibrous leaf of the pericardium, or "pulsion diverticula." Rohn[6] and Atayas-Maraty,[7] in 1885, described cystic lesions which they explained as having been formed by the pinching off of a serosal hernia of the pericardium. Grabowski,[8] in 1926, considered that since his patient had had syphilis, the lesion might be a gummatous lesion. Dufour and Mourrut,[9] in 1929, and Yater,[10] in 1931, concluded that in their cases the lesions were of lymphatic origin. Lauer,[11] in 1925, and Lambert,[12] in 1940, clearly stated the probable congenital nature of these lesions.

This paper is an attempt to clarify the concept of these cysts and to explain the occurrence of these cysts in the locations in which they are found and their relationship to certain of the diverticula of the pericardium. It is not the purpose of this paper to discuss the mechanisms which might account for changes in the mediastinum or pericardium in association with inflammatory or degenerative disease. The reader is referred to the papers of Kienböck and Weiss,[13] Cushing,[14] and Reitan[15] for extensive collective reviews of mediastinal abnormalities.

To accomplish our purpose we reviewed the cases of cysts of the mediastinum encountered at the Mayo Clinic from June, 1941, to December, 1947, inclusive, and also cysts of the mediastinum and diverticula of pericardium which were reported in the literature.

In order to limit our study to congenital lesions in both series we excluded cases in which any significant pulmonary or cardiovascular disease had been reported in the case record or protocols.

The cases accepted are grouped in Table I in accordance with the type of lesion, the site and type of attachment rather than chronologically, in order to indicate the etiologic mechanism which will be suggested. In the interest of

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TABLE I. PERICARDIAL LESIONS

LESION	AUTHORS	CASES	TOTAL CASES
Diverticulum of pericardium with wide base	Schirmer[24]	1	3
	Lauer[11]	1	
	Bristowe[25]	1	
Diverticulum of pericardium with narrow base	Peacock[26]	1	5
	Coën[5]	1	
	Neprjachin[27]	1	
	Grabowski[8]	1	
	Mazer[20]	1	
Cysts with pedicle to pericardium	Atayas-Maraty[7]	1	7
	Corsini[28]	1	
	Elinschewitsch[29]	1	
	Bradford, Mahon, and Grow[23] (Cases 5, 7, and 8)	3	
	Pickhardt[1]	1	
Cysts of the cardiophrenic angle	Yater[10]	1	17
	Cabot Case 23492[30]	1	
	Lambert (Berry and Butler)[12]	2	
	Bradford, Mahon, and Grow[23] (Cases 6, 10, 11, and 12)	4	
	Leahy and Culver[31]	1	
	Authors' cases	8	
Cysts located higher in mediastinum with no recorded attachment at cardiophrenic angle	Dufour and Mourrut[9]	1	5
	Authors' cases	4	
Total			37

brevity, the 25 cases from the literature are merely listed as details may be found in the references quoted. The 12 new cases from the clinic are reported briefly.

REPORT OF CASES

CASE 1.—A white man, 64 years old, was first seen at the clinic June 25, 1941. Chief complaint was sacral backache. Routine roentgenograms of the thorax revealed an irregularly rounded mass in the right cardiophrenic angle, which appeared to be distinctly separate from the chest wall and the diaphragm (Fig. 1). No pulsation was noticed on roentgenoscopic examination. Exploration for diagnosis of a possible sacral tumor was performed on July 4, 1941, but no tumor cells were found. On July 17, 1941, another exploratory operation was performed for a possible omental subcostosternal hernia. The diaphragm was normal, but a tumor was felt in the region of the pericardium. On Aug. 27, 1941, the mediastinum was explored and a large cystic tumor was found in the right cardiophrenic angle in the anterior mediastinum. It was adherent to the right mediastinal pleura at the cardiophrenic angle. The cyst was filled with clear fluid. Vessels were ligated in the anterior mediastinum and on the pericardium. The postoperative course was uncomplicated.

Pathologic examination revealed a thin-walled cyst, measuring 9 by 6.5 by 6.5 cm. The walls were composed of fibrous connective tissue lined by flat epithelium.

CASE 2.—A white woman, 61 years old, who was first seen at the clinic Dec. 4, 1942, gave as the chief complaint a tumor in the chest of three and one-half years' duration accompanied by exertional dyspnea and substernal pain on exertion. Roentgenographic examination of the thorax revealed an irregularly rounded mass, completely separated from the diaphragm in the right cardiophrenic angle anteriorly with its broad base to the mediastinum and the sulted a physician in his home locality and he was referred to the clinic for further investigation. Roentgenographic examination of the thorax revealed a rounded mass in the right upper part of the anterior mediastinum, slightly above the level of the aortic arch (Fig. 4). At operation, Jan. 3, 1946, a simple cystic tumor was found in the anterior mediastinum and removed. It bulged into the right side of the thorax anteriorly and superiorly and lay anterior to the superior vena cava, to which it was adherent.

Pathologic examination revealed a simple cyst, lined by a single layer of very flattened cells, resembling endothelium.

CASE 9.—A woman, 56 years old, was first seen at the clinic June 18, 1946, because of "tightening of the chest." Roentgenographic examination revealed a rounded mass at the cardiophrenic angle anteriorly, not definitely separated from the anterior wall of the chest and the diaphragm. At exploratory operation July 25, 1946, a cystic tumor, attached to the pericardium and the pleura, was found at the right cardiophrenic angle and removed.

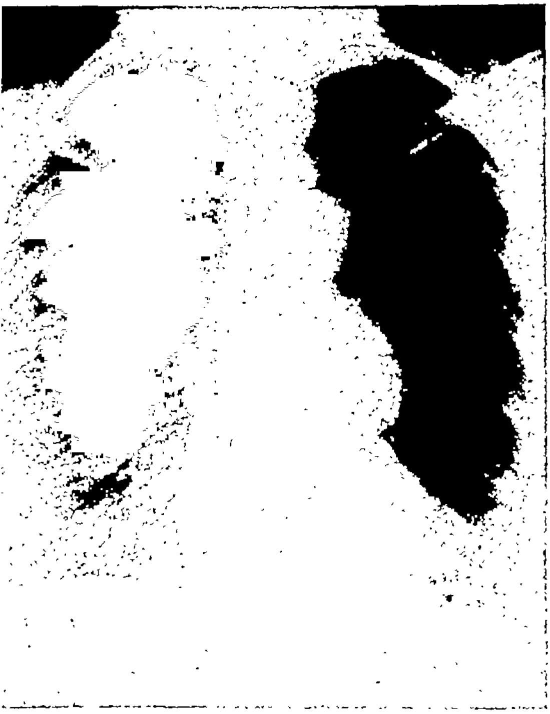

Fig. 3.

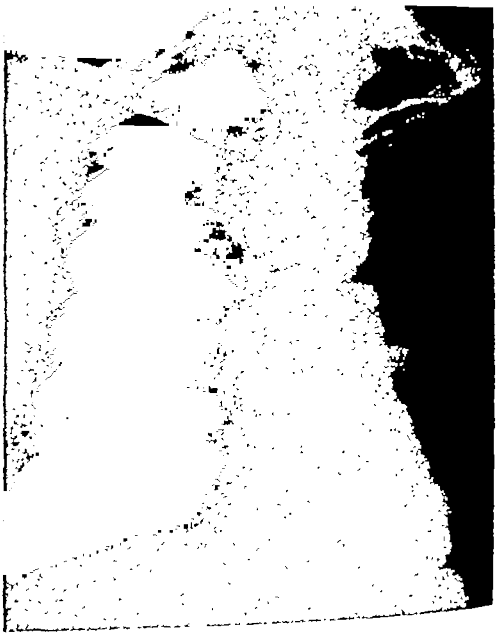

Fig. 4.

Fig. 3 (Case 7).—Cyst in left part of anterior mediastinum.
Fig. 4 (Case 8).—Cyst in right side of the anterior mediastinum.

Pathologic examination revealed a simple cyst, measuring 8 by 5 by 5 cm. and containing 115 c.c. of straw-colored fluid. The cyst was lined by a single layer of cells, resembling endothelium.

CASE 10.—A white man, 36 years old, was first seen at the clinic Jan. 20, 1947. Chief complaint was a dull pain in the right side of the thorax of two and one-half years' duration. Bronchoscopy revealed no intrabronchial tumor. Cytologic study of the sputum revealed no malignant cells. Roentgenographic examination of the thorax revealed a well-circumscribed mass located anteriorly in the right base just above the diaphragm. At exploratory operation March 15, 1947, a cystic tumor was removed from the anterior inferior portion of the thorax (Fig. 5). It was slightly adherent to the diaphragm and to the anterior portion of the pericardium.

CASE 11.—A white woman, 59 years old, was first seen at the clinic Aug. 11, 1947. Chief complaint was a chest tumor which had been discovered during a county tuberculosis survey. There were no significant symptoms. Roentgen examination of the thorax revealed a large tumor of the anterior mediastinum extending into the left pulmonary field. The tumor which was fairly well circumscribed pulsated and moved with respiration. On August 18, a cystic *tumor, containing clear fluid, was removed. It extended from the apex of the thoracic cavity* on the left to the level of the fourth rib anteriorly, where it was adherent to the pericardium.

Pathologic examination revealed a cystic tumor, filled with clear fluid, which measured 9 by 7 by 5.6 cm. and weighed 209 grams. The cyst was lined with a single layer of flattened cells.

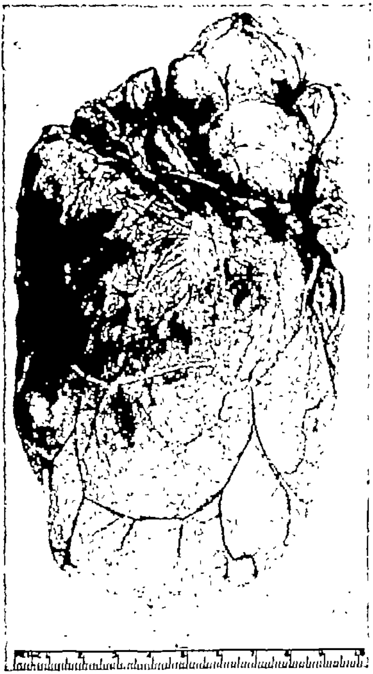

Fig. 5 (Case 10).—Cyst removed.

CASE 12.—A white man, 49 years old, was seen for the first time at the clinic Oct. 17, 1947. Chief complaint was of a chest tumor that had been found on a routine chest survey. He had had dyspnea on exertion for five years. Roentgenologic examination of the thorax revealed a mass in the *right* cardiophrenic angle. The thorax was explored Oct. 29, 1947, and a pearshaped cyst was found in the anterior mediastinum. The base was attached to the pericardium and the point was at the cardiophrenic angle anteriorly. The cyst was removed without difficulty.

Pathologic examination revealed a cyst, 7 by 5.5 by 4 cm., filled with clear fluid. The cyst was lined by a single layer of flattened cells. Chemical analysis of the fluid from the cyst showed: 50 mg. of sugar, 710 mg. of chlorides, and 0.3 Gm. of protein per 100 c.c.

DEVELOPMENT OF THE PERICARDIUM

The formation of the body cavities from the mesenchyme will be considered generally before certain aspects of the development of the pericardium. The celom arises from splitting of the lateral mesoderm on each side of the body into splanchnic and somatic layers. When the body of the embryo is folded off from the extra-embryonic membranes, the extra-embryonic and intra-embryonic portions of the celom are separated from each other. It is the intra-embryonic portion of the primitive celom which gives rise to the body cavities.

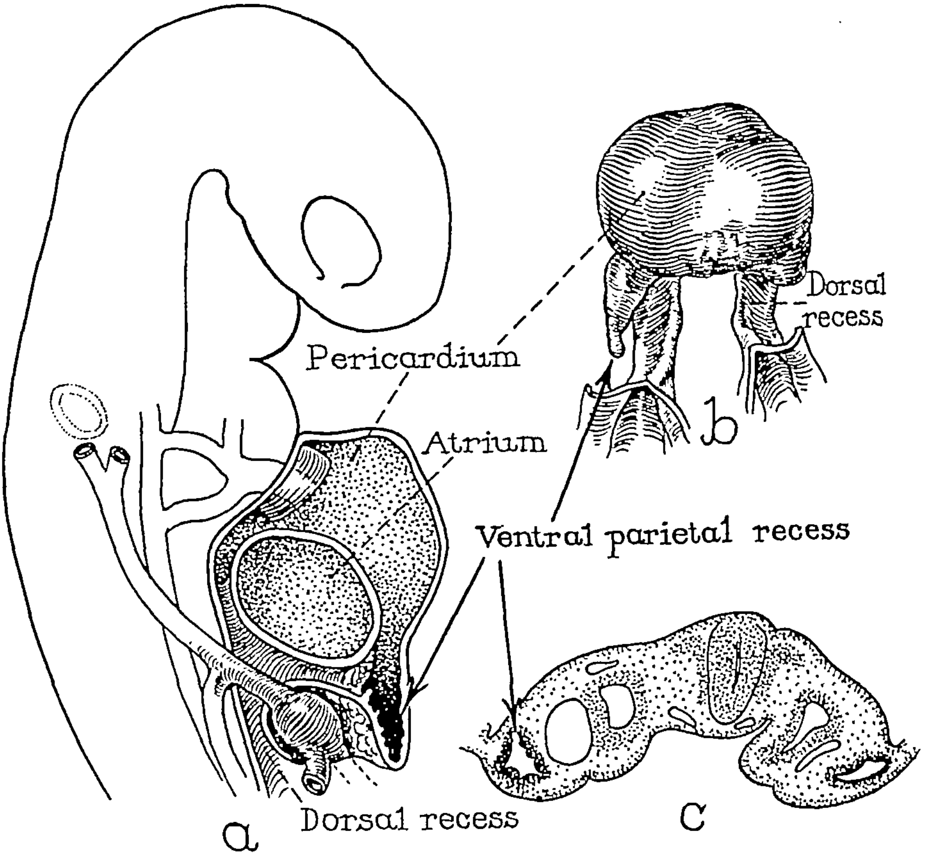

Fig. 6.—*a*, Parasagittal section of a rabbit embryo 9 days old modified from His article. The ventral parietal recess pockets into the septum transversum are illustrated. *b*, (After Davis). The ventral surface of a cast of the pericardial celom of a twenty-somite human embryo illustrating the diverticulum-like appearance of the ventral parietal recesses. *c*, (After Elliott). Transverse section of a ten-somite rabbit embryo, giving another representation of the spatial relationships of the ventral parietal recess.

The pericardial celom is the most precocious of the body cavities. It forms as a horseshoe-shaped cavity about the head of the embryo as a result of the coalescence of the mesenchymal spaces in the celomic cavities on each side of the embryo. This mechanism has had attention brought to it by Lambert.[12] The first step in the division of the body cavities comes with the coalescence of the septum transversum between the limbs of the omphalomesenteric veins from each side. The anlage of the liver forms on the caudal side of this mass, the caudal wall of the pericardium on the cephalic side.

In his original description of the formation of the pericardium and other body cavities, Wilhelm His,[16] in 1881, distinguished two pairs of recesses in the pericardial celom, which he called "the dorsal and the ventral parietal recesses of the pericardial celom." The dorsal parietal recesses are generally known as the "pleuroperitoneal canals" and their role in the formation of the pleural cavities is well understood. The ventral parietal recesses have remained obscure, probably because no significance has ever been attached to them and because they are not well defined in all embryos. However, their presence was shown in the rabbit by Elliott,[17] in 1931, and in the human embryo by Mall,[18] in 1910, and by Davis[19] in 1923. Davis stated, "Besides the pleuroperitoneal openings, the septum transversum possesses a pair of ventral recesses, described by Strahl and Carius and shown by Mall in the human embryo 21 mm. in length." Elliott[17] *stated, "With the formation of the septum transversum, the pericardial* cavity communicates caudally with the pleuroperitoneal portion of the celom by two constricted canals, the iter venosus of Lockwood or the pleuroperitoneal recesses. The pericardial cavity ends caudally in four of these recesses, the two dorsal and the two ventral pleuroperitoneal recesses—the ventral recesses end blindly at the septum transversum and only the dorsal recesses continue into the pleuroperitoneal coelom." Figure 6 *a, b,* and *c* should assist in the development of a spatial concept of the ventral parietal recesses.

RELATION OF THE VENTRAL PARIETAL RECESS TO DIVERTICULA OF THE PERICARDIUM AND TO CELOMIC CYSTS OF THE MEDIASTINUM

We were impressed by the number of cysts which were located at the cardiophrenic angle or were connected to it by a pedicle and were struck by the similarity of the structure of the mesothelial-lined cysts of the mediastinum to that of diverticula of the pericardium in cases in which there was no significant pulmonary or cardiovascular disease. The case of Mazer,[20] in which the lesion was thought even at exploration to be a cyst until it was demonstrated that *fluid could be expressed between it and the pericardium suggested strongly* that these lesions were related. Since the lesion in so many of the reported cases had a definite relationship to the pericardium at the cardiophrenic angle, it seemed possible that some mechanism other than that proposed by Lambert might be found to account for these lesions.

The discovery that a diverticulum-like structure occurred during development of the pericardium at the site where so many of these lesions were found led to speculation as to their possible relationship. With this in mind, Table II was constructed to show the several possible states in which a ventral parietal recess might be expected to persist and pairing these states with the several states of reported pericardial-celomic cysts and diverticula of the pericardium: The conclusion is difficult to escape that the relationship of the various cysts and diverticula of the pericardium to the several states of persistence of the ventral parietal recess is more than fortuitous. It seems reasonable to conclude that persistence of the ventral parietal recess may be considered as a mechanism which could account for the formation of pericardial-celomic cysts and certain diverticula of the pericardium.

TABLE II. LESIONS WHICH MAY RESULT WHEN VENTRAL PARIETAL RECESS PERSISTS

EMBRYONIC CONDITION	LESION RESULTANT
The ventral parietal recess persists Intact	Diverticulum of pericardium with wide base
Proximal portion is constricted	Diverticulum of pericardium with narrow base
Proximal portion is completely constricted	Cysts with pedicle which extends to pericardium
Is completely pinched off	Cysts in the cardiophrenic angle
Is completely pinched off and left cephalad as the septum transversum moves caudally	Mesothelial-lined cysts found higher in the mediastinum than the cardiophrenic angle

This concept is not completely at variance with the "pulsion diverticulum" theory of Rokitansky.[2] It differs in that it requires the persistence of a definite embryonic structure rather than the pinching off of a hypothetical hernia through a hypothetical weak spot in the pericardium. It has the advantages of not requiring the postulation of a change in the hydrodynamics of the heart and pericardium.

The several other possibilities of cyst formation in the development of the pericardium and pleura may be ignored because the relationship of these lesions to the development of the pericardium, as pointed out by Lambert,[12] is so definite.

PATHOLOGIC ANATOMY

Celomic cysts of the mediastinum are cysts which are composed of fibrous connective tissue, lined by a single layer of flat cells similar to serosal and endothelial cells and which contain clear yellow fluid.

These cysts are found in the anterior mediastinum, usually at one of the cardiophrenic angles. Of the 29 cysts studied (literature and our own) 17 were at the cardiophrenic angles and 7 were connected to the pericardium by pedicles from the cardiophrenic angle. Five cysts were either in the anterior mediastinum at the level higher than the cardiophrenic angles or arose in the anterior mediastinum and extended into the superior mediastinum. Of the 26 cysts for which this information is available, 17 were found on the right side and 9 were found on the left.

The content of these cysts has been described as resembling "spring water" from its translucency and clarity. The contents of several of the cysts in our series were analyzed chemically. The content of protein varied from 0.1 to 0.3 Gm. per 100 c.c., of chlorides from 693 to 710 mg. per 100 c.c., and of fats from 0 to 10 mg. per 100 c.c. The findings of low proteins, high chlorides, low sugar, and low content to absence of fat are characteristics of transudates generally, rather than of exudates or of lymph, according to the criteria of Cantarow and Trumper.[21]

None of these tumors has been found to be malignant.

CLINICAL FEATURES

The salient point in all of the histories of the surgical cases reviewed is that the lesions have been removed at exploration for a circumscribed intrathoracic lesion. A striking feature of the clinical histories is that in 15 of the 23 cases for which the information is available, the patient had no complaint other than the discovery of a tumor during routine roentgenologic examination of the thorax. Six of the patients complained of epigastric or precordial pain and 2 complained of tachycardia. It is apparent that no symptom complex can be ascribed to the presence of these tumors.

In no case was the lesion suspected as the result of general physical examination.

Roentgenographic Aspects.—In 15 of the 25 cases in which information on the roentgenographic aspects was available the diagnosis of a mediastinal lesion was made as a result of routine roentgenologic examination of the thorax.

Of the lesions for which reports of the roentgenologic examination were available, 18 were on the right side and 7 were on the left. Of the lesions on the right side, 14 (78 per cent) were situated in the region of the cardiophrenic angle and of the lesions on the left side, 3 (42 per cent) were at the cardiophrenic angle. In 17 cases (68 per cent) of the 25 the lesions were located at the cardiophrenic angles.

Lesions in the cardiophrenic angles presented a fairly characteristic appearance. They were well demarcated, rounded or elliptical in form, and homogeneous in density. The lesions followed no rule in separation from the anterior chest wall or from the diaphragm.

Differential Diagnosis.—In no instance has a definite diagnosis of pericardial-celomic cyst or diverticulum of pericardium been made before operation. The reader is referred to the classifications of Heuer and Andrus[22] and of Bradford, Mahon, and Grow[23] for comprehensive review of lesions to be considered in the differential diagnosis of lesions of the mediastinum.

In 2 of the cases in this series, the possibility of a diaphragmatic hernia of the foramen Morgagni type was considered. Inasmuch as the lesions are at the same site, and may have a similar cause, confusion seems inevitable.

Diagnosis and Treatment.—The exact diagnosis of pericardial-celomic cyst or pericardial diverticulum has been made at thoracotomy in the recent cases and at post-mortem examination in the earlier cases. No operative deaths have been reported, and there is no published record of significant postoperative morbidity.

SUMMARY

A collective review of the literature was made for cases of cysts of the mediastinum, filled with a clear fluid and lined by mesothelium and of diverticula of the pericardium in persons who did not have any associated systemic disease which could reasonably have been supposed to have caused these abnormalities. Twelve new cases of pericardial-celomic cysts found in the files of the Mayo Clinic were reported.

The development of the pericardial celom has been reviewed and emphasis placed on the role that persistence of the ventral parietal recess of the pericardial celom may play in the development of these cysts and diverticula.

It has been pointed out that diverticula of the pericardium and celomic cysts of the mediastinum may represent stages in the same developmental process and that they may be considered in this light rather than as separate clinical and pathologic entities.

It is suggested that the exact diagnosis of these cysts and diverticula will continue to be made at surgical exploration since there are no definite diagnostic criteria.

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Original Communications

STUDIES WITH ARTERIOVENOUS FISTULAS

I. RESPONSE OF THE NORMALLY INNERVATED AND DENERVATED HEART TO OCCLUSION OF THE FISTULA

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THOUGH the medical profession was slow in becoming aware of the remote effects of arteriovenous fistulas upon the circulatory apparatus in general and of the possible harmful effects upon the heart in particular, once interest was aroused the circulatory dynamics in this condition were studied intensively both in experimental animals and in man. In spite of the important contributions which have been made, however, certain important facets of the problem remain obscure. In a study of patients with arteriovenous fistulas carried out during the last war Elkin and Warren[1] were able to make certain physiologic observations, including ballistocardiographic estimations of cardiac output. It was a striking fact that not only was the response of pulse rate and blood pressure almost instantaneous but the reduction in cardiac output similarly began immediately upon compression of the fistula. Because of the startling rapidity with which reduction in stroke volume occurred and the lack of alteration in right atrial pressure, Elkin and Warren reached the conclusion that "it appears to be a nervous reflex related to the sudden change in resistance against which the heart must pump."

The present communication deals with efforts to determine whether sympathetic denervation or both sympathetic and vagal denervation of the heart alters the response to digital occlusion of an arteriovenous fistula. It was hoped that this study would throw some additional light upon the mechanism of this response. It was also realized that any information which might clarify the circulatory dynamics associated with arteriovenous fistulas might promote a better understanding of the function of the heart and circulatory system in general and the influence of various stresses and strains.

From the Department of Surgery, Indiana University School of Medicine.

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TABLE I. RESPONSE OF CARDIAC OUTPUT AND BLOOD PRESSURE TO DIGITAL OCCLUSION OF ARTERIOVENOUS FISTULA IN DOGS WITH NORMAL CARDIAC INNERVATION, SYMPATHETIC DENERVATION, AND TOTAL EXTRINSIC DENERVATION OF THE HEART

NUMBER OF ANIMAL	STUDY OF CARDIAC OUTPUT BEFORE CREATION OF A-V FISTULA	LENGTH OF FISTULA IN CM.	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND STUDY OF CARDIAC OUTPUT	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND SYMPATHECTOMY	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND POSTSYMPATHECTOMY STUDY OF CARDIAC OUTPUT	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND STUDY OF CARDIAC OUTPUT AFTER VAGOSYMPATHETIC DENERVATION	RESPONSE OF CARDIAC OUTPUT TO OCCLUSION OF FISTULA			BLOOD PRESSURE RESPONSE TO OCCLUSION OF FISTULA
							NORMAL CARDIAC INNERVATION	SYMPATHETIC DENERVATION	TOTAL CARDIAC DENERVATION	
1	Yes	2.0	3.0	7.0	8.0	8.5 / 9.0	good	good	good	good
2	Yes	1.8	2.5 / 3.5	6.0	6.5	7.0	good	good	good	good
3	Yes	1.2	2.5	3.0	4.0	5.0	poor	varied	good	good
4	Yes	1.1	0.7	1.0		1.5	good		poor	good
5	Yes			0	0.2			good		fair
6	Yes	3.0	0.2	0.7	1.5	1.7	poor	good	varied	fair
7	Yes	3.4	1.5 / 2.0	2.0	2.5	2.5	good	good	good	good
8	Yes	2.0*	0.3	1.0	1.5	1.5	poor	poor	varied	poor
9	Yes	2.5*	0.7 / 1.2	2.0		2.2	varied		good	poor
10	Yes	3.4	0.5	1.5	1.7	1.7		good	good	good
11	No			0	0.2	0.2		poor	good	poor
12	No	5.5		1.5	1.7			good		good
13	No	2.2	8.0	8.0	8.0	8.0	good		good	good
14	No	3.0	7.0	7.0	7.0	7.0	good		good	good
15	No	1.6	7.0	7.0	7.0	7.0	good		poor	good
16	No	2.0	7.0	7.0	7.0	7.0	poor		poor	good
17	No	2.5	8.0	8.0	8.0	8.0	good			good

*Proximal vessels found to be occluded at post-mortem examination.

In Table I are briefly summarized the results of the study. In 10 animals the cardiac output was determined before creation of a fistula. The length of the fistula as measured at post-mortem examination ranged from 1.1 to 5.5 cm.; unfortunately the records of the length of the fistula in 2 dogs were lost. Listed also are the time intervals between the creation of the fistula and the subsequent procedures of measurement of cardiac output, sympathetic denervation, determinations of cardiac output after sympathectomy, and the final determinations after interruption of the vagosympathetic trunks. It will be noted that approximately one-half of the studies were completed within 2½ months after production of the fistula, while the other one-half were delayed 7 to 8 months. The response of the cardiac output to occlusion of the fistula was listed as good in those cases in which a significant decrease occurred. The response was listed as poor when either a slight decrease or a frank increase in cardiac output occurred and as varied when the results of duplicate or triplicate determinations were conflicting. The instantaneous changes in blood pressure following occlusion of the fistula are also tabulated. It will be noted that in 2 animals exhibiting no rise in blood pressure upon digital compression and in which the responses of cardiac output were more or less at variance with the majority of observations, the proximal artery and vein of the fistula were found to be occluded at the time of post-mortem examination though the fistulas were patent. The record of the condition of the fistula at the time the animal was sacrificed was unfortunately lost in a third instance in which there was no rise in blood pressure and in which the cardiac output rose slightly upon compression of the fistula on one occasion. In 3 dogs (No. 1, 2, and 5) several blood volume determinations were made before and after the fistula was created. In dog number 1 values beforehand were 124 and 131 c.c. per kilogram of body weight. Two months after the fistula was made the blood volume was 149 and 2 months later was 175. In the case of dog number 2 the preoperative blood volume was 101 c.c. per kilogram and 4 months after the fistula was made it was 125. The preoperative values were 105 and 110 in dog number 5 while 2 months after the fistula was produced the blood volume was 135 c.c. per kilogram.

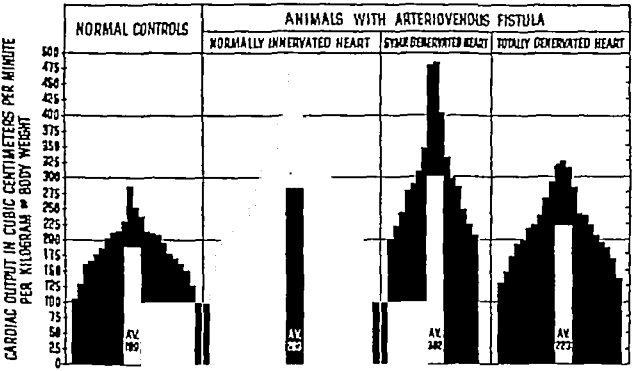

Fig. 2.—Values of cardiac output in normal dogs, in dogs with an arteriovenous fistula, and in such animals after sympathetic and total extrinsic cardiac denervation.

In Fig. 2 are charted the values for cardiac output in normal dogs and in dogs following the production of an arteriovenous fistula and the subsequent operations for denervating the heat. There were 22 apparently valid determinations of cardiac output in 17 normal dogs in 10 of which studies were subsequently made after the production of a fistula and after cardiac denervation. These 22 determinations, when expressed in cubic centimeters per minute per kilogram of body weight, ranged from 103 to 287 and averaged 189. In three fourths of them the values ranged from 150 to 230 and also averaged 189. In 13 dogs, in which fistulas had been established from 7 days to 3 months, 29 determinations of cardiac output gave values ranging between 168 and 495 c.c. per minute per kilogram of body weight, the average being 283. Only four of these estimations were below 210. Sixteen determinations of cardiac output were made from one week to 8 months after the production of the fistula in 9 animals in which sympathetic denervation had been carried out. These values ranged from 200 to 484 c.c. per minute per kilogram of body weight and averaged 302; only 2 were below 220. In the last group of 13 dogs with fistulas ranging in age from one week to 9 months and in which the vagal and sympathetic fibers to the heart had been interrupted, 22 determinations of cardiac output gave values varying from 147 to 320 and averaging 223; 5 were below 200.

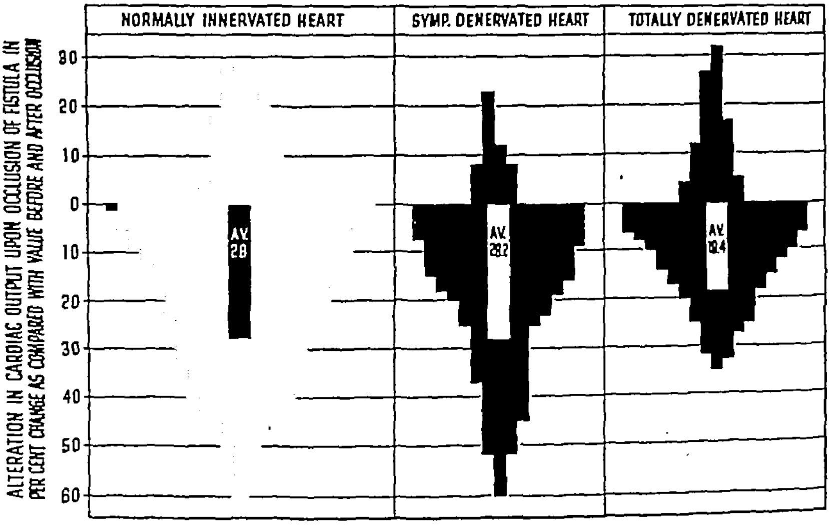

Fig. 3.—Alterations of cardiac output upon complete digital occlusion of the arteriovenous fistula in dogs with normally innervated, sympathetically denervated, and totally denervated hearts.

The alterations in cardiac output upon occlusion of the fistula are illustrated in Fig. 3; they are expressed in per cent change from the value determined immediately before or after occlusion. Thirty determinations of the response of cardiac output were made upon 13 dogs with normally innervated hearts. In 77 per cent a decrease occurred, the average reduction in cardiac output being 28 per cent. Following sympathetic denervation of the heart, occlusion of the fistula caused a decrease in 79 per cent of the tests; the average reduction in cardiac output was again 28 per cent. When the vagosympathetic trunks were sectioned and the fistula was occluded a decrease in cardiac output occurred in a comparable number of studies (74 per cent), the average decrease being 18.5 per cent. From Table I it will be observed that a decrease in cardiac output upon digital compression of the fistula occurred in 8 of 13 animals with normally innervated hearts (61.5 per cent), while the response was variable in one additional dog, making a decrease in output an invariable or occasional occurrence in 9 of the 13 (69 per cent). If those animals are excluded in which a significant rise in blood pressure did not occur upon occlusion of the fistula, a decrease in cardiac output was noted in 8 of 11 (73 per cent). In those dogs in which a sympathetic denervation had been performed a decrease in cardiac output occurred upon occlusion of the fistula in 7 of 10 (70 per cent) while one additional animal responded variably; thus a decrease occurred invariably or on occasion in 8 of 10 (80 per cent). If those animals are excluded in which a significant rise in blood pressure was not noted upon compression of the fistula, a decrease in cardiac output was observed in 7 of the 8 animals (88 per cent). Such a response occurred on one but not both tests in the eighth dog studied. Following complete denervation of the heart a decrease in cardiac output upon occlusion of the fistula was observed in 9 of 14 animals (64 per cent) and a decrease was noted on occasions in 2 additional dogs; thus such a response occurred at times in 11 of the animals (78 per cent). If those dogs are excluded in which a significant rise in blood pressure was not observed during occlusion of the fistula, 7 of 11 animals exhibited a decrease in cardiac output (64 per cent) and a decrease occurred in one but not both tests performed upon another. Hence a decrease was noted invariably or on occasion in 8 to the 11 (73 per cent).

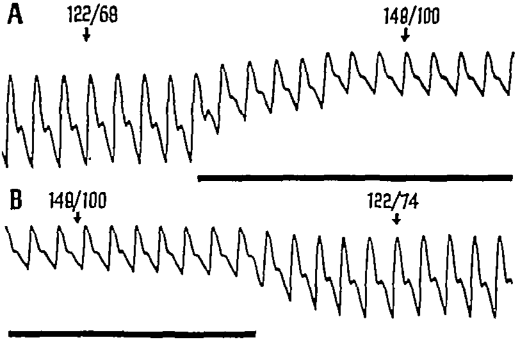

Fig. 4.—Optically recorded Hamilton manometer measurements of the change in blood pressure (*A*) upon occlusion and (*B*) upon release of pressure from the arteriovenous fistula in dog 3. The blood pressure rose from 122/68 to 148/100 with occlusion and upon release fell to 122/74. The pulse rate remained constant at 96 per minute. The period of occlusion is indicated by the heavy line. The record is actually a continuous one. At the time the study was made the complete extrinsic nerve supply to the heart had been interrupted.

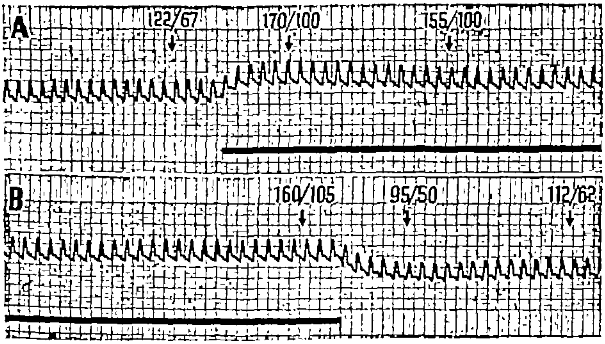

Fig. 5.—Electromanometric recording of alterations of blood pressure (*A*) upon occlusion and (*B*) upon release of compression of arteriovenous fistula in dog 16. The blood pressure rose from 122/67 to 170/100 upon occlusion, leveled off a few seconds later at 155/100, and then rose slightly to 160/105. Upon release of compression the blood pressure fell to 95/50 and quickly leveled off at 112/62. The pulse remained constant at 100. The period of occlusion is indicated by the heavy black line. The record is actually a continuous one. At the time this study was made the total extrinsic nerve supply to the heart had been interrupted.

Three and one-half months after the fistula was made, in the case of dog number 2, cardiac output was determined before and after digital occlusion of the fistula and then after exposure and precise ligation of the proximal vein. The output decreased from 4,400 c.c. per minute beforehand to 2,280 c.c. during digital occlusion. It was reduced to a comparable degree immediately after ligation of the proximal vein (2,660 c.c. per minute) even though there were present large venous collateral vessels and a strong continuous thrill persisted. Two months later the cardiac output had risen to the neighborhood of 5 liters per minute and digital occlusion brought about a striking reduction in output.

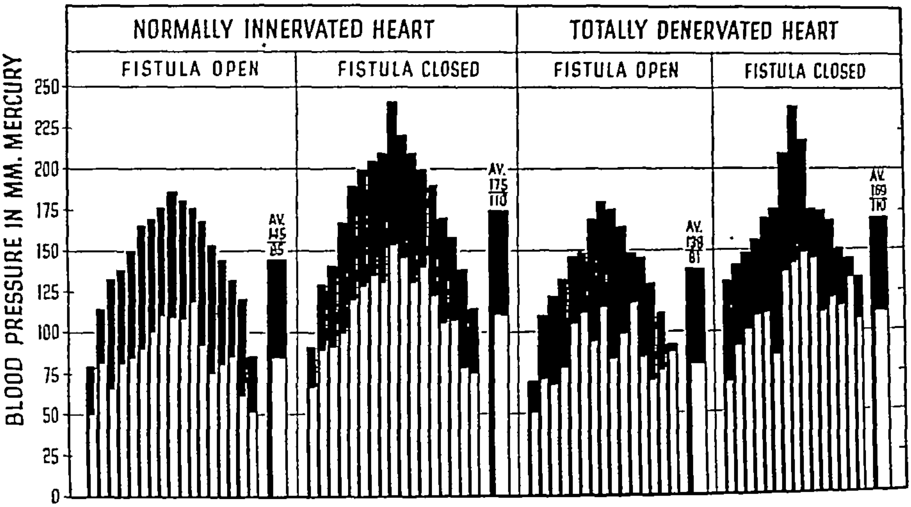

Fig. 6.—Values of systolic and diastolic blood pressure before and during occlusion of an arteriovenous fistula and in dogs with normal cardiac innervation and in dogs with total cardiac denervation.

There was a prompt rise in blood pressure upon occlusion of the fistula in 14 of the 17 animals studied and in 12 of them the elevation in pressure was marked. It is of some interest that of the 3 animals which did not exhibit this characteristic change in blood pressure, in 2 the proximal artery and vein connected with the fistula were observed to be thrombosed, even though the fistula was patent when examined after the animal was sacrificed, while our notes concerning the condition of the fistula at post-mortem examination were lost in the third instance. A rise in both systolic and diastolic pressure was noted. The change in blood pressure was repeatedly observed to occur with the very first beat of the heart after the fistula was compressed (Figs. 4 and 5). The peak of the elevation in blood pressure always occurred within 3 seconds after which it began to level off, reaching in approximately 20 seconds a plateau which remained considerably above the level observed before occlusion of the fistula (Fig. 4). In these figures is also illustrated the rapid reversal which takes place upon release of pressure from the fistula. The same type of change in blood pressure occurred regardless of whether the normal innervation of the heart was left undisturbed, whether its sympathetic fibers had been removed, or whether it had been totally denervated. In Fig. 6 are charted observations of alterations in blood pressure upon occlusion of the fistula in animals with normally innervated and totally denervated hearts. It can be seen that these changes are comparable in the two groups not only qualitatively but also quantitatively.

DISCUSSION

The studies reported would indicate that the characteristic decrease in cardiac output and elevation of blood pressure upon digital occlusion of a peripheral arteriovenous fistula take place regardless of whether the heart is normally innervated, deprived of its sympathetic innervation, or totally denervated. The bradycardiac reaction observed in man does not occur in the dog asleep with pentobarbital. It is recognized that the method for estimation of cardiac output employed, though reasonably accurate, is nevertheless subject to some experimental error and that maintenance of the same basal status for all studies is difficult to achieve. It would be interesting to repeat these studies using another method for estimating cardiac output, for example, ballistocardiography. There can be no question about the accuracy of the blood pressure observations. Altogether, it would appear evident that the observations recorded constitute overwhelming evidence that the response of cardiac output and blood pressure follow the same pattern irrespective of the preservation or interruption of the extrinsic innervation of the heart.

We have assumed that removal of the sympathetic chain from above the caudal cervical ganglion down to below the fifth or sixth thoracic ganglion effectively interrupts all the sympathetic fibers to and from the heart. On gross examination we have not demonstrated any sympathetic fibers passing to the heart from any other portion of the sympathetic chain. Certainly this conclusion might be reached in man from the persistent bradycardia which follows extirpation of the chain from above the stellate ganglion to below the fourth or fifth thoracic ganglion, as well as from the relief of anginal pain when the same portion of the chain is removed. The interruption of vagal fibers in our studies was obviously complete. We have, of course, used the word total denervation in reference to the extrinsic nerve supply of the heart only.

Explanation of the prompt and dramatic decrease in output of the denervated heart upon occlusion of an arteriovenous fistula can be adequately accounted for according to the law propounded by Starling for control of the output of the heart. From studies of heart-lung preparations, he observed that the output of the heart was dependent solely upon the volume of input and was independent of the blood pressure against which the left ventricle must empty its load. His conclusion that the output was related to the input and more specifically to the degree of stretching of ventricular fibers has withstood the test of time. In the case of our experiments with complete extrinsic denervation of the heart of otherwise intact animals, the sequence of events can be explained as follows: The sudden occlusion of the fistula interrupts the immediate return to the heart of that relatively large volume of blood which has previously been returned directly from the fistula through the proximal vein. Thus, with the very next diastole of the heart, a reduced volume of blood enters the right atrium and subsequently the right ventricle. With the reduced input, the ventricular fibers are not stretched to the point which characterized the previous diastole and consequently a reduced volume is ejected with systole. Though the previous volume may still have passed into the left ventricle and been ejected from it with this first stroke, in the succeeding diastole the reduction is at play in left atrial and left ventricular input and the output necessarily becomes equal to the output from the right side. The reduced cardiac output continues to maintain a comparative reduction in filling and emptying of the heart. Some idea of the significant reduction in the volume of blood returned to the heart immediately upon digital occlusion of an arteriovenous fistula is evident from other studies concerned with rotametric determination of the volume flow of blood through the proximal vein under various circumstances.[3] Blood flow values through the proximal vein have varied from 15 to approximately 75 c.c. per minute per kilogram of body weight, the average being in the neighborhood of from 30 to 35 c.c. per minute per kilogram. This flow is reduced to zero when the fistula is occluded digitally. It should be pointed out that the fistulas in this group were smaller than those in the animals used in the present study. It will be recalled that the values for total cardiac output in our animals with open arteriovenous fistulas averaged from a low of 223 c.c. per minute per kilogram in one group to a high of 302 c.c. per minute per kilogram in another. Furthermore, in at least one instance ligation of the proximal vein alone effected an immediate reduction in cardiac output of comparable degree to that brought about by digital occlusion of the fistula.

Other studies which we have carried out have not demonstrated any elevation above the normal range of right atrial pressure in dogs with open arteriovenous fistulas. Though the pressure in the femoral vein opposite the fistula is as high as arterial pressure, the pressure gradient rapidly falls and pressures are normal in the distal portion of the inferior vena cava. Moreover we have not demonstrated any significant alteration in right atrial pressure upon digital occlusion of the fistula.

The cardiac outputs in animals with open fistulas and complete interruption of the extrinsic cardiac nerve supply were not as high as in those with intact cardiac innervation or in those with sympathetically denervated hearts.* Explanation of this difference is not clear and further study of the problem is contemplated.

The elevation in blood pressure with occlusion of the fistula and its decrease with release of compression of the fistula may possibly be the result of the interplay of a number of factors, but it can be explained satisfactorily solely upon the sudden alteration in peripheral resistance. It is an interesting fact that the sudden occlusion of an arteriovenous fistula not only brings about a decrease in cardiac output but also an elevation in blood pressure. This means that the work done by the heart during the period immediately following compression of the fistula is not lowered in a degree comparable to the reduction in cardiac output. It is well known, however, that with passage of time after obliteration of a fistula the elevated blood pressure drops to a lower level and with this change would occur a diminution in the work load of the heart.

The demonstration that the characteristic response of cardiac output and blood pressure to the opening and closing of a peripheral arteriovenous fistula is essentially the same, regardless of the presence or absence of extrinsic cardiac innervation would lead one to believe that the response of the heart to other changing stresses may also be more dependent upon mechanical factors than upon extrinsic nervous regulation. We have been impressed with the importance of initiating other experiments designed to elucidate this and related problems.

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*When the cardiac outputs in animals with open fistulas are compared statistically with those of normal dogs, the T score is found to be highly significant in the group with intact cardiac nerves, in that with sympathetically denervated hearts, but not definitely significant in that with totally denervated hearts. Yet in approximately 75 per cent of each of these 3 groups a decrease in cardiac output occurred upon digital compression of the fistula.

SUMMARY AND CONCLUSIONS

1. Studies are reported demonstrating that the characteristic decrease in cardiac output and increase in blood pressure upon digital occlusion of an arteriovenous fistula take place in dogs with sympathetically denervated hearts and in dogs with total interruption of their extrinsic cardiac nerves as well as in animals with normally innervated hearts.

2. The change in cardiac output upon opening or closing an arteriovenous fistula is explained according to Starling's law upon alteration in the volume input and consequent differences in the stretching of the ventricular muscle fibers. The change in blood pressure would appear to be explainable upon the alterations in peripheral resistance.

The authors wish to express their appreciation to Dr. N. N. Stahl and Dr. E. E. Wayson for their help with the initial studies performed.

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EXPERIENCES WITH THE EXPERIMENTAL SURGICAL RELIEF OF AORTIC STENOSIS

A Preliminary Report

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THE therapeutic problems posed by the presence of chronic valvular disease of the heart have alternately stimulated and baffled the combined ingenuity and daring of both physician and surgeon for many years. The possibility of a direct surgical approach has been particularly intriguing to the surgeon, especially when the valve has become stenotic in character. As stenosis is essentially a mechanical stricture, its relief must logically be sought by mechanical (surgical) means. Undoubtedly struck by a similar conclusion, Tuffier,[1] in 1914, successfully attempted surgical relief of a stenotic aortic valve. The patient was a young man who had shown signs of a marked and progressive aortic stenosis. The thorax was opened and the root of the aorta exposed. It was the operator's intention to insert a knife above the aortic ring and to incise the stenosed valve, but the procedure was changed to a dilatation of the aortic valve by invaginating the wall of the aorta just above the valve and pushing its wall into the stenosis on the forefinger. As late as 1924, this patient was reported living and improved. To date no other definitive surgery upon the human aortic valve has been reported.

Emboldened by a reasonable measure of success with the surgical alleviation of mitral stenosis, it was natural that attention should be turned toward its counterpart in the aortic valve. Our interest in this phase of valvular surgery was initiated by the enthusiasm and efforts of the late Horace Smithy, whose untimely death resulted from the rapid devastation of the disease under discussion. It became apparent at once that the lessons learned and the approaches employed in the development of mitral surgery could not be transposed in toto to the aortic valve because of the latter's variation in anatomic structure and relationships to vital coronary pathways. Nevertheless, certain broad patterns for investigation suggested themselves as a result of experiences encountered in this earlier experimental and clinical phase of valvular surgery.

PATHOLOGIC AND PHYSIOLOGIC CONSIDERATIONS

The pathology of aortic stenosis is varied and complex. It appears that the primary defect in the rheumatic type is an early fusion of the valve cusp margins. The free edges of the valve cusps are thickened, rolled, and eburnated.

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They may actually contain calcium but even in its absence are extremely hard and tough. The valve leaflets themselves vary greatly but are invariably thickened and in most fixed specimens appear rigid and unyielding. In extreme cases the entire aortic valve may be considered as a rigid orifice surrounded by a calcified plaque having lost all semblance of its original tricuspid nature. The fresh specimen, however, frequently reveals a considerable amount of flexibility of the cusps themselves, especially near their attachments to the aortic wall. In this respect the pathology resembles that found in the average case of mitral stenosis (Figs. 1 and 2).

Stenosis of the valve thus described does not seem actually to involve the aortic wall itself. Bell[2] has pointed out that intimal atherosclerotic changes of the ascending aorta are invariably absent in these cases. He feels that the so-called degenerative aortic stenosis is actually only a late form of the initial rheumatic lesion in which calcium deposition plays a prominent role. He has demonstrated in a large autopsy series numerous transition stages between undoubted rheumatic and calcific stenosis. Associated mitral disease, myocardial Aschoff bodies, and other rheumatic stigmas are practically the rule in carefully investigated cases of "degenerative" aortic stenosis. Thus available evidence supports the rheumatic origin of nearly all cases of this disease. Even in clear-cut rheumatic cases calcification is common. It may merely thicken and indurate the valve edges and the cusps themselves, or it may extend down one or more commissures (fused valve edges) into the immediately adjacent aortic wall. In some cases it then extends as a long stalagmite of limestone nearly free in the aortic lumen except for its lateral attachment. The orifices of the coronary arteries are located approximately one centimeter above the two anterior valve cusps. Rarely, if ever, do they become involved or distorted by the disease process originating within the valve (Figs. 3 and 4).

The disturbed physiology in extreme aortic stenosis is apparently due to the slow ejection of a relatively small amount of blood with each contraction of the left ventricle. As a result the systolic blood pressure does not reach high levels but is sustained and maintained longer than is usual. Diastolic pressures likewise are relatively high, so that the pulse pressure differential is small. Coronary flow is probably reduced more by the diminished volume of blood in the aorta than it is by either pressure changes or intrinsic disease in the coronary system itself. Naturally, the coronary vascular needs of the left ventricle are increased by virtue of the large bulk of musculature contracting partly isometrically against the aortic obstruction. This extra work load increases the relative inadequacy of the coronary flow and thus probably explains the "anginoid" or "coronary" type of pain so often seen in these cases.

Patients with uncomplicated aortic stenosis are not dyspneic unless congestive failure has supervened. They become progressively disabled as their cardiac stroke output diminishes with increasing stenosis. Eventually even the slightest exertion produces dizziness and fainting. Persistence in exertional efforts leads to greater discrepancy between supply and demand, both sys-

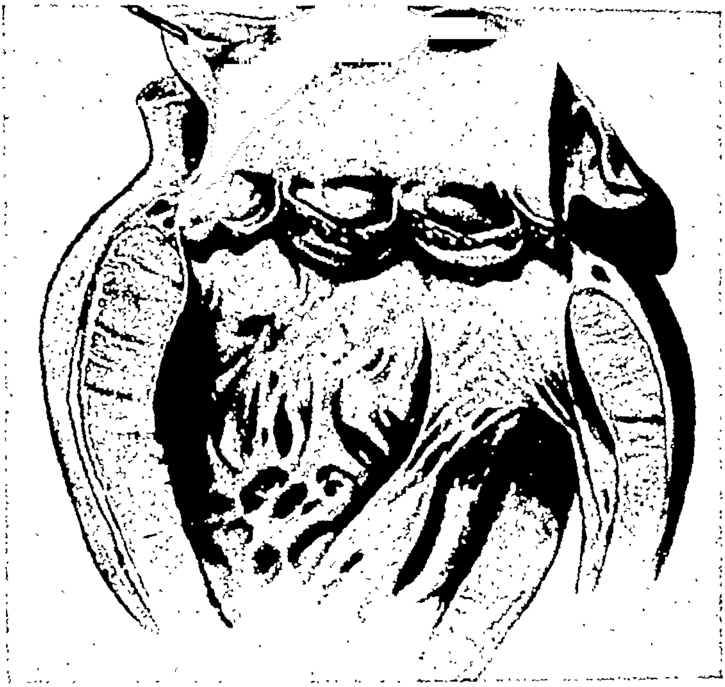


Fig. 1.—Rheumatic vegetations on free edges of aortic valve cusps.

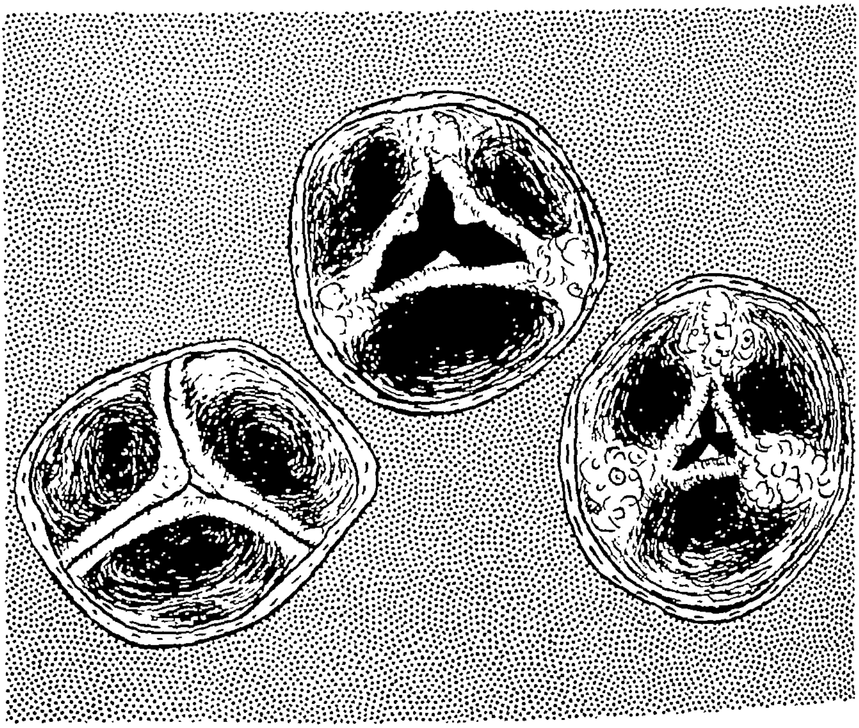


Fig. 2.—Progressive fusion of adjacent valve cusps at the commissures.

tomically and with regard to coronary flow. In all probability this may explain the relative frequency of sudden death which so often follows rather moderate effort in cases with this type of lesion.

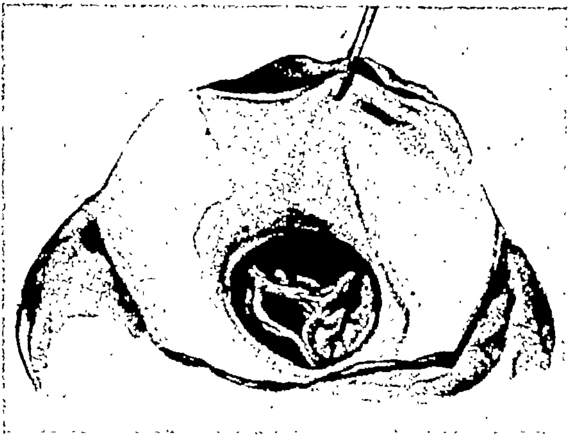


Fig. 3.—Typical and basic pathology of aortic stenosis.

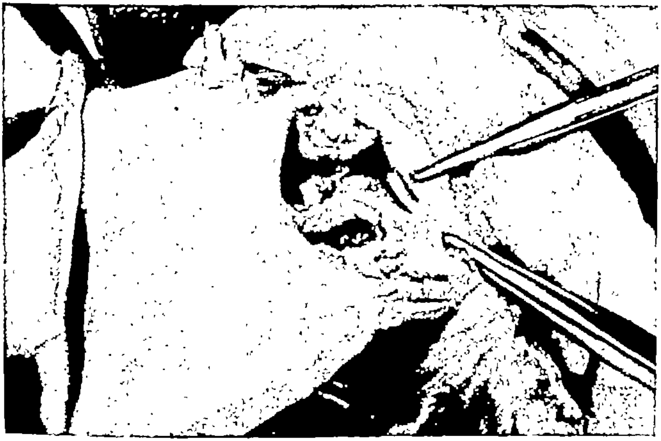


Fig. 4.—Extreme anatomic distortion of aortic valve by fibrosis and calcification. Even here considerable flexibility is usually observed in the fresh specimen.

EXPERIMENTAL CONSIDERATIONS

The approach to the problems of stenotic valvular disease in the experimental laboratory is fraught with many difficulties. The experimental animal does not have valvular stenosis, nor can a reasonable facsimile of the human pathologic picture be produced by methods yet devised. Therefore, animal experimentation cannot follow the usual accepted form, but resolves itself into methods of surgical technique designed either to approach the valve itself or to by-pass it by involved methods of vascular anastomoses. Study of human heart specimens obtained at autopsy is likewise unsatisfactory because they usually represent extreme states of disease—a distortion of the conditions which may exist at the time when surgery could reasonably be contemplated. Further, because fixation of the tissues has destroyed certain important functional components such as mobility, bizarre conclusions are drawn.

The first reaction of the authors following a study of preserved specimens of aortic stenosis was that only an entirely new valve could offer a reasonable solution. The obvious conclusion to such an observation lay in three directions: (1) the insertion of a mechanical valve or (2) the replacement or (3) by-passing of the damaged valve by a section of transplanted aorta containing normal valves.

1. It is possible that plastic valves may eventually be developed for the replacement of normal aortic valvular function. Such a valve has been employed experimentally by Hufnagel[3] and Campbell.[4] Whether this valve or others embodying the same principle will be satisfactory is open to question. They are inserted into the aorta beyond the coronary ostia, thus violating the normal relationship between valve and coronary. Normally, with a competent valve, coronary flow is maintained by the head of pressure within the aorta during ventricular diastole. The physiologic effects of this reversal of position will require intensive study, but would seem to be a serious objection to this type of approach.

We have had no experience with prosthetic valves. Our initial experimental attempts, however, employed a somewhat similar principle using homologous body tissues. The concept was to excise a portion of stenotic valve and replace valve action by an inverted vein graft similar to the technique used by Murray[5] in mitral valve surgery.

Using mongrel dogs, the external jugular vein was removed and turned inside out to present an endothelial surface to the blood stream. A segment of tendon was then passed through the inverted vein to lend it substance. A specially prepared cork borer was then passed through both aortic walls near its root at the myocardium. The prepared vein graft was drawn through the lumen of the borer, which was then withdrawn, leaving the graft transfixing the aorta. Purse-string sutures in the aortic wall prevented bleeding about the openings. However, the great depth of the aortic valve within the heart substance required such a long graft loop that efficient valvular function and diastolic tamponade was not obtained. Attempts to insert the graft within the myocardial portion of the aorta failed because of the proximity of the coronary vessels (Figs. 5, 6, and 7).

2. Direct valve grafts using small segments of aorta and pulmonary artery with their contained valves met with a similar fate, primarily from massive hemorrhage. One animal survived the procedure and the valve graft became intimately attached to the aortic ring. However, the valve did not function because of distortion of its cusps. The great dangers associated with these maneuvers led us to discard, at least temporarily, this idea of direct valve transplantation.

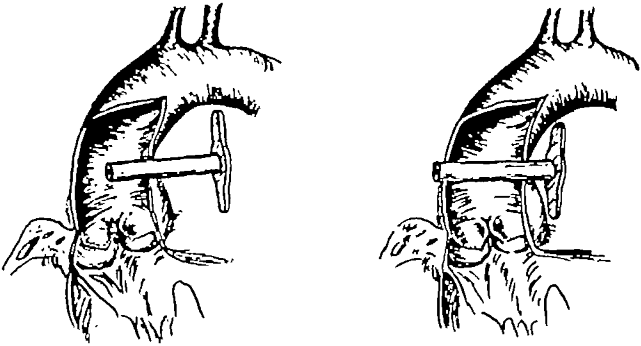


Fig. 5.—Passage of cork borer through both aortic walls.

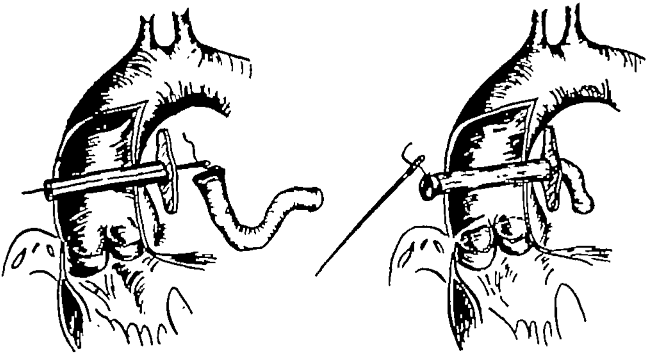


Fig. 6.—Passage of inverted vein graft through cork borer.

3. A. Methods of by-passing the aortic valve using free grafts of aorta were then explored, utilizing two methods of approach to the left ventricle. First the aortic valve, aortic arch, and descending thoracic aorta were removed en masse from sacrificed dogs. All tributary vessels along the course of the aortas so obtained were ligated. The aorta was then divided into two separate

grafts by severing its continuity just below the left bracheocephalic artery. The distal end of the valve-bearing graft was then anastomosed by end-to-side technique to the descending aorta using the Potts-Smith aortic clamp method. After release of the aortic clamp the grafts became distended with blood and pulsated. The three transparent valve cusps approximate perfectly and restrain blood flow without leakage. The other graft segment from the descending aorta was then anastomosed end-to-end to the valve-bearing end of the pulsating graft, thereby obtaining additional length toward the left ventricle.

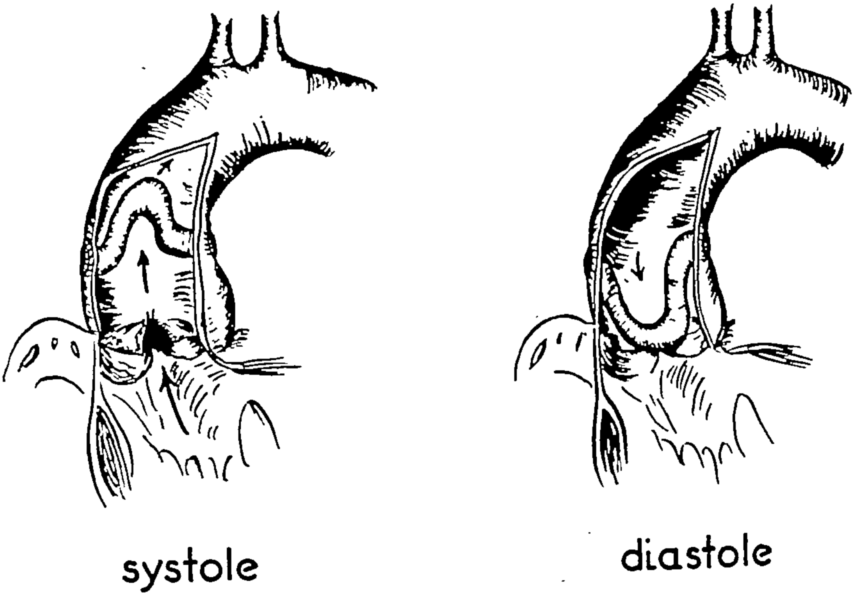


Fig. 7.—Movement of vein graft. Tamponade of valvular defect during diastole.

A site for insertion of the free end into the left ventricular cavity was then selected at a point away from the coronary vessels, mitral valve, and its papillary system. The free end of the graft was inserted into the left ventricle through a stab wound using four silk sutures fastened to the quadrants of the graft. These sutures were passed from within the ventricular lumen outward through the cardiac wall. Hemorrhage between graft and myocardium was controlled by purse-string suture in the myocardium and interrupted sutures as needed.

This technique was attended by an excessive operative mortality from hemorrhage, ventricular fibrillation, and mitral insufficiency due to the inclusion of chordae tendineae in the sutures. In addition, essential hemostatic purse stringing in the myocardium may partially or completely occlude the orifice of the graft within the left ventricle. Of eight dogs subjected to this technique, only one survived more than a few days.

B. An improvement in the technique consisted in using a somewhat longer portion of the descending aorta for the graft. This portion of the graft could then be passed through a cylinder of Polythene of appropriate size and long enough to extend completely through the ventricular wall. The free end of the graft was then drawn back over the Polythene to form an endothelialized cuff completely over the tube. Because of the rigidity of this portion of the prepared graft, it was easy to insert into the ventricular lumen, and more adequately to control bleeding by simple tightening of the myocardial purse string. Simple suturing of epicardium and graft was sufficient to securely hold it in place (Figs. 8, 9, and 10).

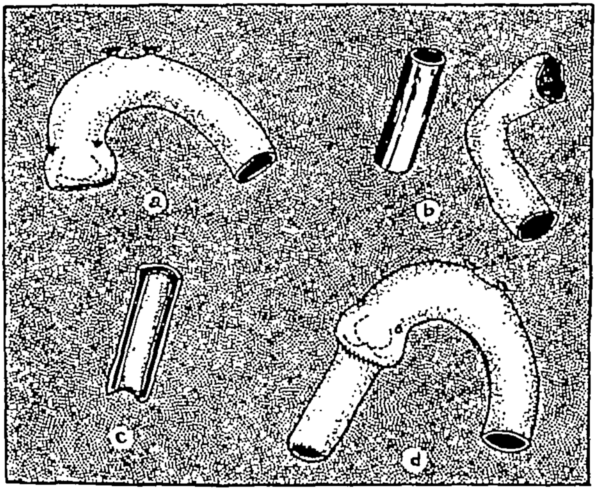


Fig. 8.—Preparation of double aortic graft including the aortic valve and incorporating a cylinder of Polythene in its proximal segment.

While this technique was superior in that hemorrhage was better controlled, in that obliteration of its lumen could not take place, and in that no great quadrant sutures were necessary to draw the graft into the ventricle, thus protecting the coronaries and chordae tendineae, not one of our twelve dogs survived. It appeared that the deaths were not due to the actual surgical maneuvers but to some grave physiologic disturbance produced by the by-pass. There was no doubt that the shunt functioned as shown by clamping it distally and incising it just proximal to the clamp. Whether the double ventricular outlet provided too easy escape of the ventricular output, thus relieving the muscular work load, or whether by-passing the coronary mouths in some way impaired myocardial function, the hearts slowed down, became feeble, and soon ceased to contract, immediately after removing a clamp placed across the middle of the graft. Prompt replacement of this clamp permitted some of the animals to improve but every time it was removed the phenomenon of the failing heart was repeated.

It is conceivable that the human heart with clinical aortic stenosis might better withstand the establishment of a second aortic outflow tract, but on the basis of these results obviously clinical trial was out of the question.

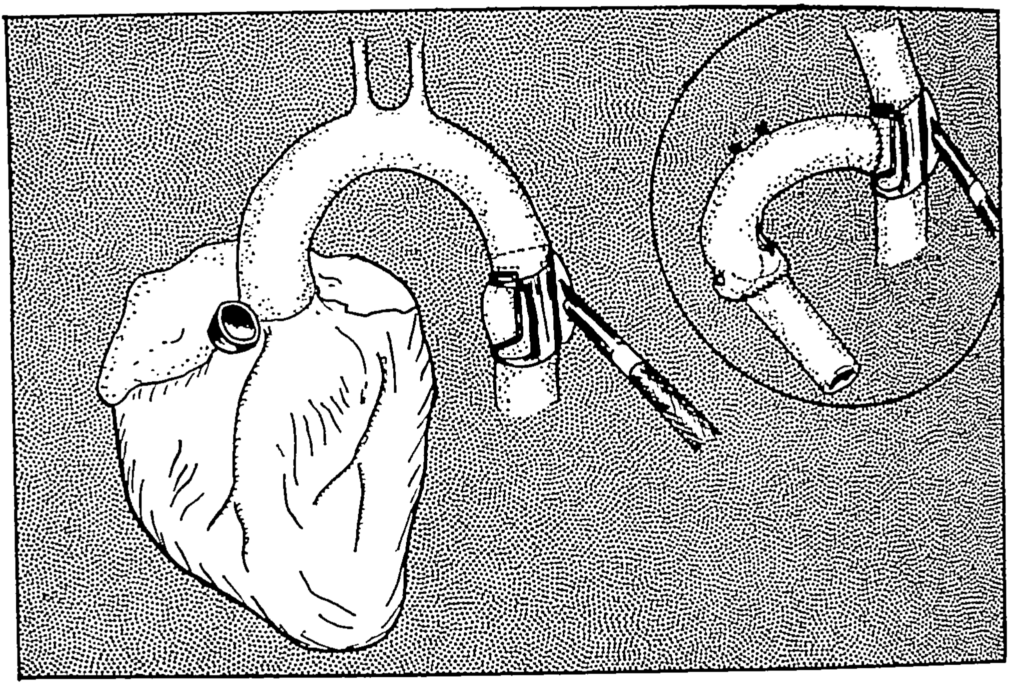


Fig. 9.—Anastomosis of distal end of graft to descending aorta using the Potts-Smith clamp and technique.

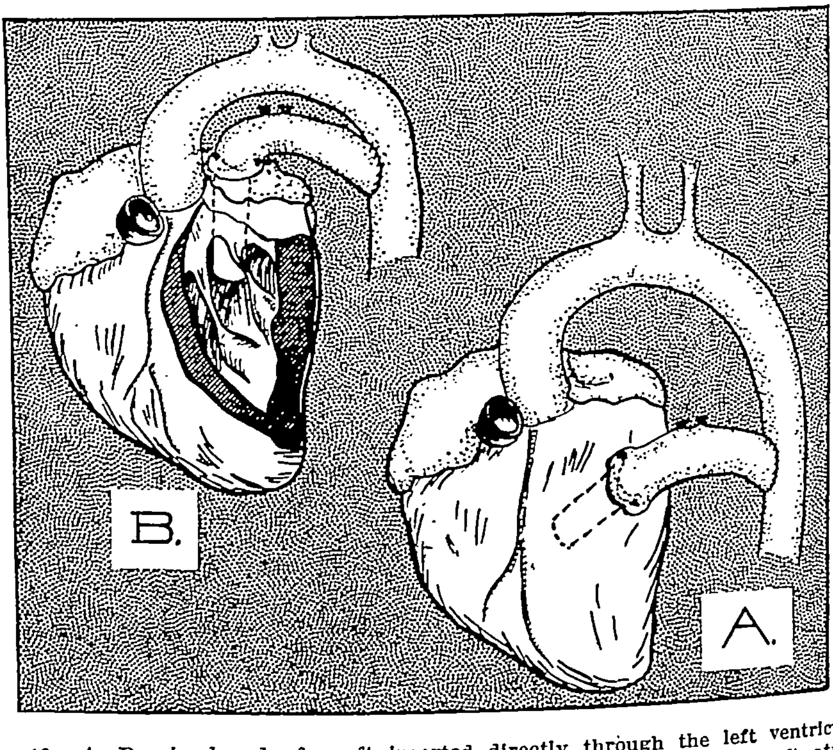


Fig. 10.—*A*, Proximal end of graft inserted directly through the left ventricular wall. *B*, Proximal end of graft inserted through left auricular appendage, left atrium, and mitral valve, to enter the left ventricular chamber.

C. It did occur to us, however, that the heart might be better able to tolerate a second aortic outflow tract if less major insult were made upon the myocardium itself. From our experiences with mitral valve surgery using the left auricular appendage to approach first the auricle, then the valve, and then actually to insert a finger and instrument into the left ventricle, we felt that a somewhat longer graft incorporating a longer tube of Polythene might well be inserted into the left ventricle by this route. The flexible mobile normal mitral valve cone would be large enough to permit insertion of a fairly large tube and would accurately close and grip it during ventricular systole, much as it grips the exploring finger. Therefore, longer grafts were prepared, and the free ends were inserted into the left ventricle via the auricle. There was no technical difficulty in seven dogs so operated. All survived at least twenty-four hours. However, a good flow through the graft such as obtained when the direct ventricular route was used was only intermittently obtained. It appeared that the ventricular wall or septum would encroach upon and intermittently occlude the orifice of the tube. In spite of the use of curved tubes and tubes with lateral openings, reliable constant blood flow through the graft was not obtainable. This may have been the reason the double aorta was better tolerated by this technique than by the direct ventricular approach. The smaller size of the distal end of the tube, necessitated by the limited size of the mitral orifice and by the smaller lumen of the lower aorta, would also tend to limit the physiologic disturbances due to a double ventricular output.

However, there was an observed tendency to sudden death among these animals while apparently in satisfactory health even several weeks after surgery. Autopsy disclosed complete thrombosis of the tube in all but one of the animals, but no other clear-cut cause of death. We presumed that the rigid tube lying in the ventricular chamber in close approximation to the septum was able to stimulate and produce various arrhythmias, eventually culminating in sudden death.

Discouraged by these attempts at by-passing or replacing the aortic valve, our efforts were redirected toward punch resection of the aortic valve. It was possible to pass a backward-cutting punch through the left ventricle up through the aortic valve, and to engage and remove a piece of the valve. In each case a typical thrill of aortic regurgitation was produced, accompanied by visible enlargement of the ventricle. Four dogs treated in this fashion survived the procedure but twelve died within twenty-four hours. When examined, a good sized defect of one of the cusps was evident in each case. However, we were impressed by the complete destruction of that cusp and questioned whether the technique would be applicable clinically. Certainly a high grade of aortic regurgitation would be a most undesirable result in human surgery.

Approach to the aortic valve by way of the innominate artery (bracheocephalic in dogs) is quite feasible. A forward-cutting punch of suitable size can readily duplicate the procedure performed through the ventricle. Six dogs were subjected to this procedure with one death. Again the amount of regurgitation produced by this method was most impressive and suggestive of its inapplicability to human cases (Figs. 11 and 12).

Smithy and Parker[6] apparently deemed an approximately equivalent amount of regurgitation produced by a hooklike instrument inserted through either the aortic or ventricular wall to be acceptable even in human patients. Of this we have grave doubt. They felt that the ventricular approach was preferable because of greater ease in controlling hemorrhage and in performing vascular repair than possible by the aortic approach. We believe that the innominate (bracheocephalic) artery is preferable to either, and even more readily controlled and repaired. We were unwilling to accept the idea of punch excision of the valve in a human patient, basing our objections in part on the following line of reasoning.

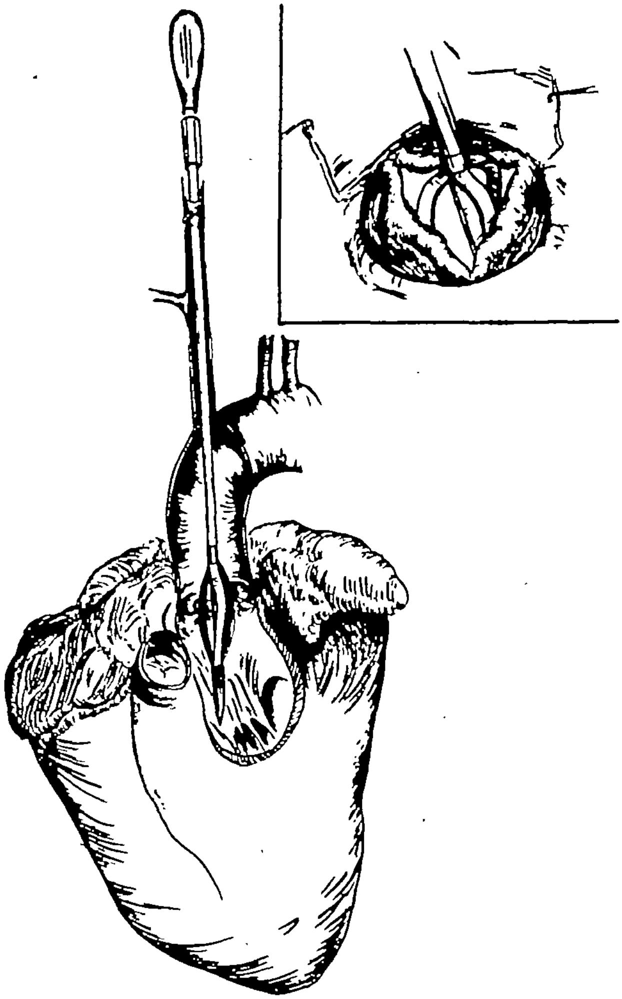


Fig. 11.—Simple incision of aortic valve cusp by innominate approach. Inset shows probable effect upon a stenotic valve.

In human aortic stenosis the lumenal passage through the valve becomes reduced, eventually to a small triangular or irregular central opening unable to open or close completely in any phase of the cardiac cycle. Regurgitation is therefore an inherent minor component of true stenosis. However, some stenotic valves are seen in which considerable motion of the edges of the aortic slit does seem possible. Such valves present even more difficulty in attempts at direct surgical correction, since having had no pre-existing regurgitation and having an enormously hypertrophied left ventricular wall with a lumenal capacity reduced below normal, they are poorly equipped to compensate for any aortic regurgitation which might be suddenly produced during surgery. Certainly regurgitation can only be compensated for by dilatation of the left ventricular chamber sufficient to expel at each contraction an amount of blood equal to that necessary for the maintenance of an adequate circulation plus the amount lost from the aorta by regurgitation through the valve. The tremendous hypertrophy of the myocardial musculature seen in clinical aortic stenosis would not seem to readily lend itself to such rapid and extreme dilatation.

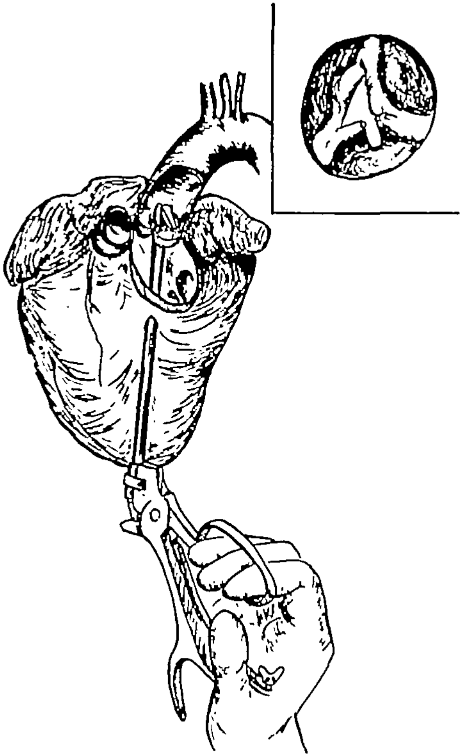


Fig. 12.—Resection of portion of valve cusp using backward cutting punch and the ventricular approach. Only four of sixteen dogs so operated survived. Each of these four exhibited remarkable and prompt dilatation of the left ventricle. This dilatation was effectively compensatory for the suddenly produced regurgitation.

Recently we have become familiar with the Brock technique for direct division of the pulmonic valve in congenital stenosis.[7] We have used the direct technique in six cases of cyanotic heart disease with excellent results. In pulmonic valve stenosis the three cusps of the valve have apparently become agglutinated or fused during fetal life into a valve cone with a tiny orifice at its apex. Only a trickle of blood can pass into the pulmonary circulation. Usually another defect exists to shunt the right ventricular blood into the systemic circulation. Brock passes a flat diamond-shaped knife through an incision in the right ventricular wall, through the stenotic valve, dividing it into two halves. In other words, the valve cone formed by fusion of the three valve cusps is divided into a bicuspid valve. Pulmonary valves are occasionally naturally bicuspid and function without evident regurgitation. Postoperatively we have been unable to detect regurgitation in our cases, and Brock does not mention it (Figs. 13, 14, and 15).

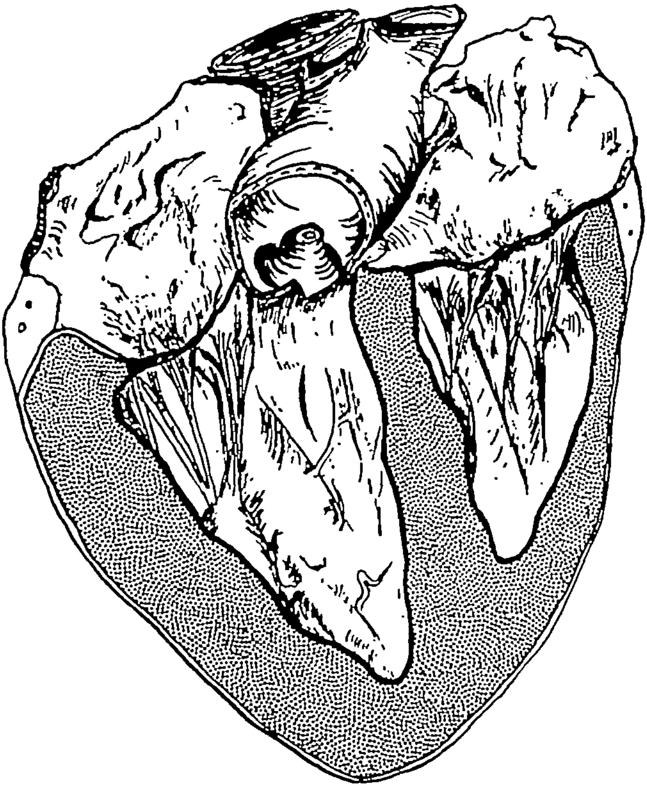


Fig. 13.—Typical pathology of congenital stenosis of the pulmonary valve.

Since the pulmonary and aortic valves are similar in construction and in method of action, we conceived the idea of performing a comparable operation for aortic stenosis. If we could produce a bicuspid aortic valve in spite of fibrosis and calcification, we felt that the strong left ventricle would force it open during systole, and that its very rigidity would prevent regurgitation during diastole. There were, however, certain important extra considerations necessary in comparable surgery within the left ventricle.

First, it seemed unbelievable that life could be maintained more than a few seconds if an incision were made in the left ventricle comparable in size to that used in the right. Therefore, we constructed an instrument with a suitable curve, 3/16″ in diameter, with retractable diamond-shaped cutting blades near its apex. *It required only a tiny puncture wound for insertion through* the ventricular wall (Fig. 16).

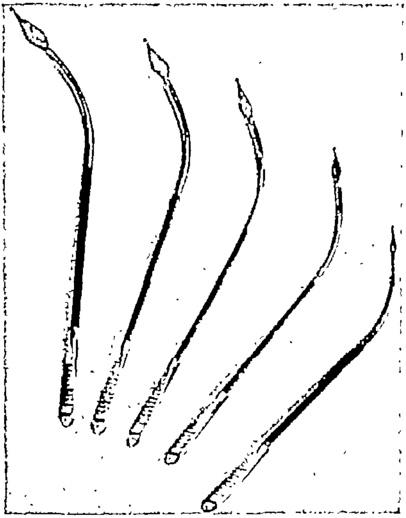


Fig. 14.—Brock-type flat valvulotomes.

Second, the presence of the coronary ostia just above the two anterior aortic valve cusps suggested a possible danger. If any inadvertent regurgitation were to be produced by surgery, it would probably be preferable that it take place through the posterior cusp. Otherwise, the rapid flow of regurgitating blood past one or other coronary orifice would markedly interfere with coronary flow during the normal diastolic filling period. Therefore, the retractable blades were placed in such a manner as to cut vertically rather than horizontally as in the Brock technique. Many specimens of aortic stenosis were studied to permit the instrument to be placed so that the upper blade would cut open the anterior commissure, or zone of fusion of the two anterior (coronary bearing) aortic cusps. The posterior blade would then cut across the center of the posterior (noncoronary) cusp. The valve should then be divided into an essentially bicuspid valve (Fig. 17).

CASE REPORT

After employing this technique on several dogs and cadavers merely for orientation, we felt that the method was applicable clinically. Therefore, on March 9, 1950, at the Episcopal Hospital, F. B., a 26-year-old white woman, unable to climb four steps without extreme dizziness, was subjected to operation. She had suffered from anginal pain even at rest for over a year. Blood pressure averaged 96/88. Pulse was regular at 80 per minute. She had a typical systolic aortic murmur and thrill and moderate cardiac enlargement.

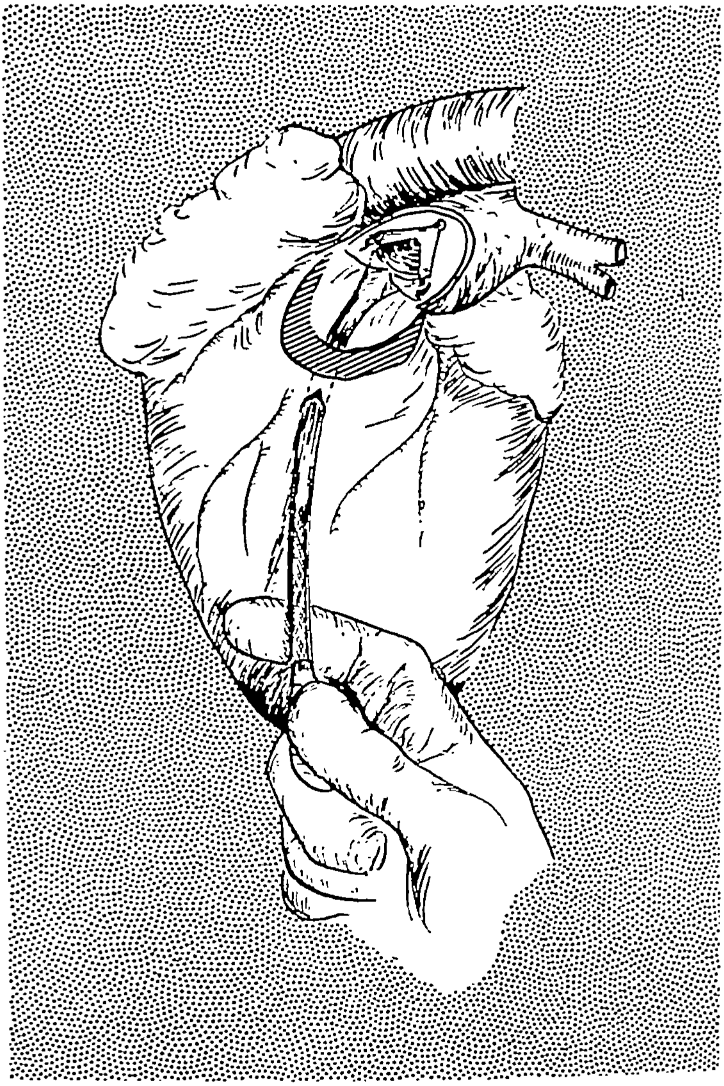


Fig. 15.—Division of stenotic valve cone into bicuspid pulmonary valve. Such bicuspid valve do not exhibit marked regurgitation.

With the patient in the supine position, the usual left inframammary incision was made. The thorax was entered through the fourth left interspace. Ribs four and five were spread and the costal cartilages were divided. The pericardium was widely opened anterior to the left phrenic nerve after flooding it with 5 per cent procaine. The point of the myocardium selected for insertion of the special retractable knife was infiltrated with 0.5 per cent procaine.

A purse-string suture and two mattress-stay sutures were placed about the selected point—1 inch above the ventricular apex and ¾ inch to the left of the anterior descending coronary artery. A small stab wound was made and the medium-sized retractable knife was inserted into the ventricular lumen. It was gradually passed up along the ventricular septum to the

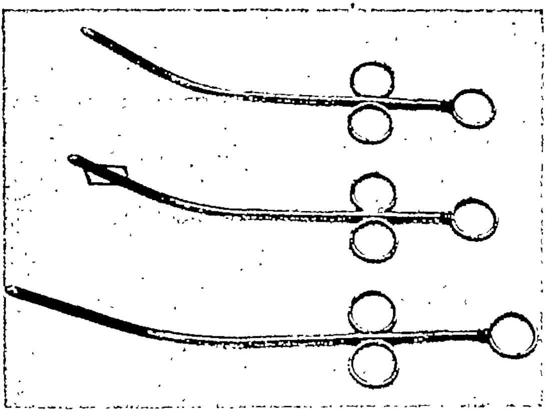


Fig. 16.—Special valvulotomes with retractable blades for anteroposterior division of fused aortic valve.

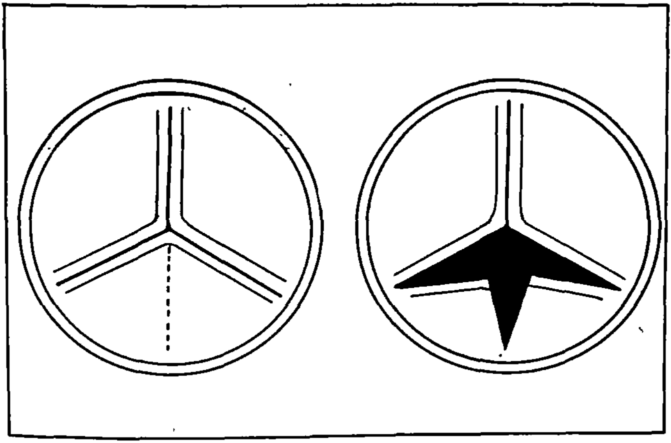


Fig. 17.—Proposed line of division of aortic valve—through the commissure between the two anterior or coronary bearing cusps and across the posterior cusp.

region of the aortic valve. Soon the calcified areas of the valve were palpable by the instrument, but the lumenal opening appeared to be most difficult to find and enter. After many unsuccessful attempts to pass the instrument through the valve, the patient's condition seemed unsatisfactory and the instrument was withdrawn to permit the heart to rest. Bleeding was controlled with difficulty because the myocardium seemed to be very friable and unsuitable for tying of sutures. However, the very thick myocardium soon stopped the bleeding spontaneously.

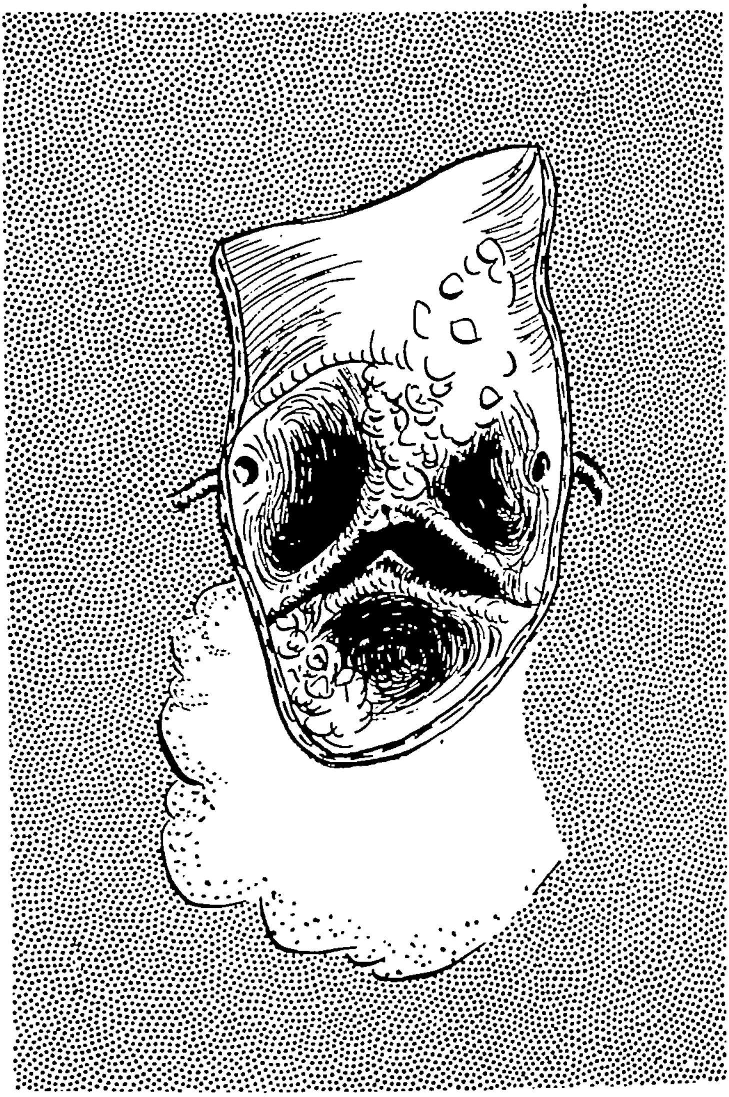


Fig. 18.—Actual pathology existing in human case at the time of surgery. Note heavy calcification in the region of the anterior commissure.

Strong cardiac contractions returned, and we considered other methods of resolving the problem. One of the difficulties in aortic surgery is the inability to see readily the diseased valve, either by direct vision or by the tactile or "digital" vision which we have employed in surgery of the mitral valve. However, both in dogs and in human beings it is sometimes possible to feel the aortic valve momentarily by the "Ramirez maneuver." With the patient supine, the surgeon stands on the right side of the table and inserts his left index finger

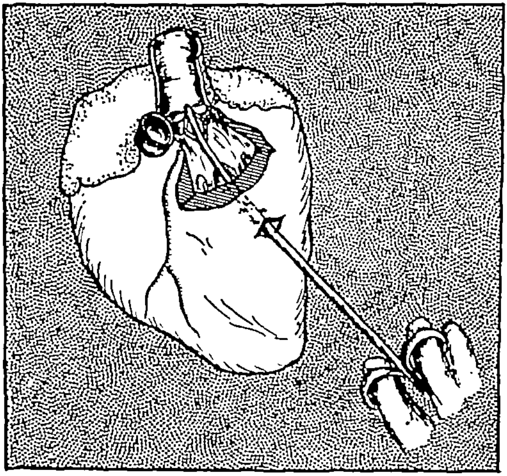


Fig. 19.—Division of human aortic valve.

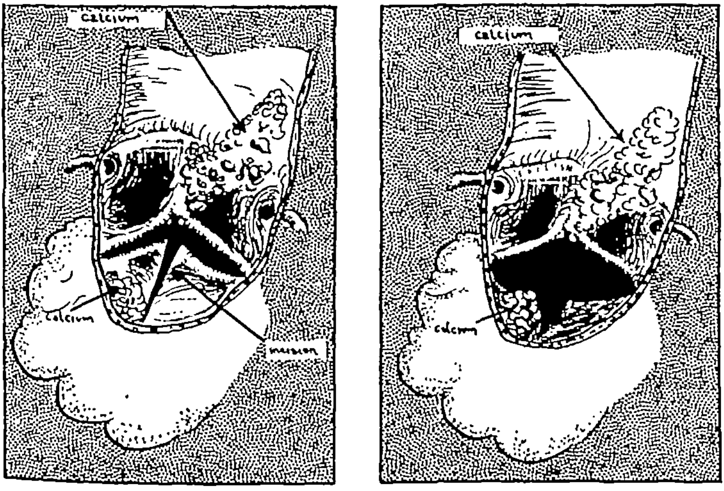


Fig. 20.—Actual line of division of human aortic valve. The calcified anterior commissure was only slightly cut. The posterior leaflet was divided.

through an incision in the left auricular appendage. The finger is then passed through the mitral valve and is bent back sharply to palpate the aortic valve. It is conceivable that actual digital dilatation of the aortic valve could be carried out in this manner.

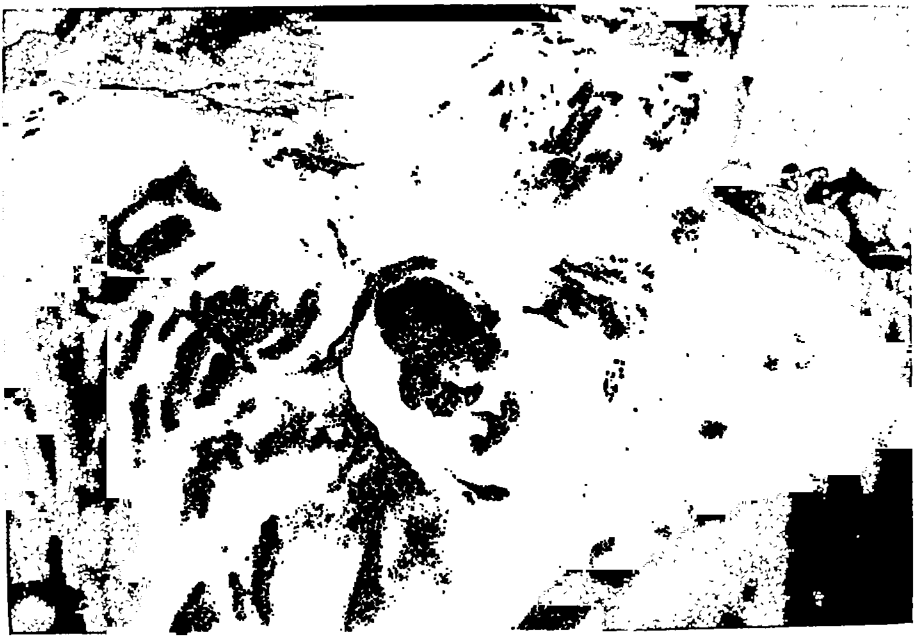


Fig. 21.—Ventricular aspect of divided aortic valve.

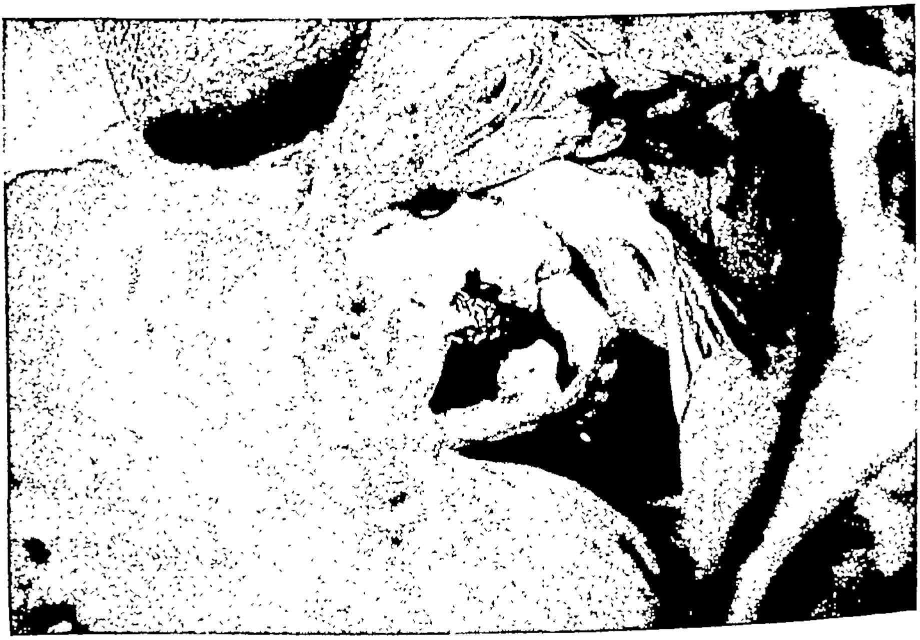


Fig. 22.—Showing regurgitant effect of division of this same valve which manifested a surprising amount of flexibility.

An attempt was made to perform this maneuver. However, the left auricular appendage in this individual with no mitral valve disease was too small to permit the index finger to enter the auricle beyond the first joint. On the other hand, had there been mitral disease the auricular appendage would have been large, but the narrowed mitral orifice would scarcely have permitted the insertion of a finger into the ventricle without severe obstruction of the auriculoventricular blood flow.

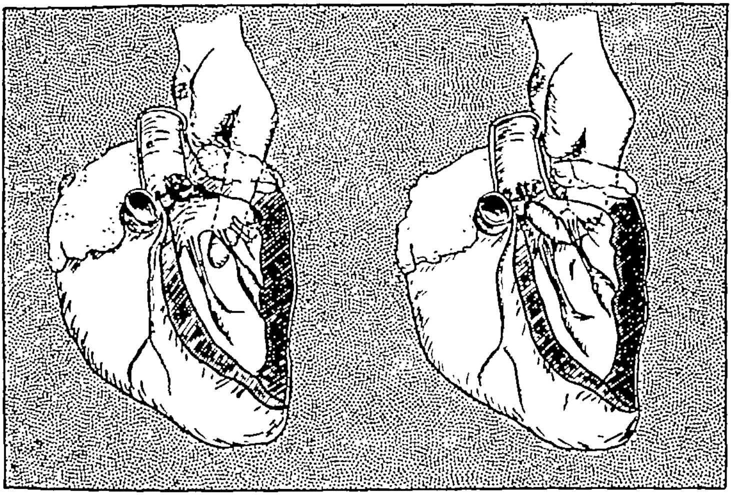


Fig. 23.—Ramirez maneuver for palpation of the aortic valve. The finger is inserted through the mitral valve via the left atrium and appendage.

After closing the auricular appendage it was determined that another attempt should be made to cut the aortic valve by the modified Brock method. The instrument was again inserted into the left ventricle and after some probing passed up into the aorta. The retractable blades were opened and the valve was cut by pulling the instrument back into the ventricle. Great resistance was met, but the instrument was finally pulled through in a partially opened position. Immediately the heart became slow and began to fail. The instrument was withdrawn and the myocardial defect rapidly sutured. In spite of stimulation, rapid transfusion, and prolonged cardiac massage, only a very transient heartbeat could be re-established. It was notable that in the dying state the left ventricle did not become dilated although the other chambers rapidly became enormous. Perhaps this inability of the left ventricle to dilate because of its great muscular hypertrophy is responsible for the frequency of sudden death in cases of aortic stenosis.

Autopsy revealed that the knife had been well placed. The anterior blade had engaged accurately upon the anterior, unfortunately calcified, commissure and had penetrated 3/16 inch through pure calcium. The posterior blade had cut directly across the middle of the posterior cusp for ¼ inch completely dividing the hard eburnated edge. It was evident from the specimen that appreciable regurgitation had been produced by division of this cusp. An amount of regurgitation far less than that tolerated by healthy dogs had been incompatible with life when superimposed upon diseased tissues (Figs. 18 to 23).

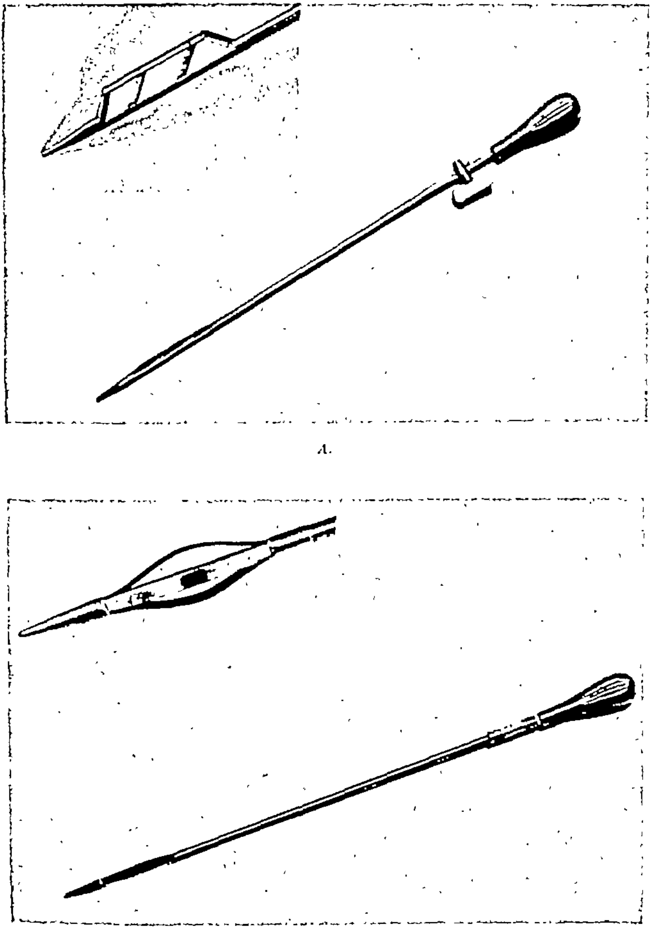
The idea of creating in effect a bicuspid aortic valve without producing regurgitation at least in this instance seemed untenable. The fresh heart specimen revealed only an average amount of pathologic change when compared with fixed specimens. The valve displayed a considerable degree of flexible, though thickened, tissue in two of the cusps and at two of the fused commissures. Because of this flexibility the interruption of the hard posterior valve edge presumably led to immediate fatal regurgitation. Division of the fixed specimens with their artificially hardened cusps had not suggested the probability of regurgitation.

Shocked and saddened by this turn of events, we have abandoned the idea of further attempts at cutting the valve for the time being. It would be eminently desirable to cut accurately the fused commissures of the stenotic valve, but this can only be done under clear vision. None of the various artificial heart-lung extracorporeal systems has as yet been perfected sufficiently to permit exclusion of the human heart from the circulation. Cardioscopic or other means of direct visualization are not yet feasible during surgery of the aortic valve.

In the meantime we have channeled our efforts in another direction. Digital dilatation of the mitral valve is not without value in the treatment of mitral stenosis. Indeed, the first truly successful effort at the treatment of mitral stenosis made by Souttar, in 1925,[8] was a simple digital dilatation using the auricular approach. More recently Brock, as well as the authors, has occasionally performed digital dilatation alone for mitral stenosis. The difficulty is that tearing will occur in the line of least resistance, which may or may not be in a favorable location. The mitral valve with heavy calcified lips invariably tears at one or both commissures, producing in effect a planned commissurotomy, but as a rule limited by the size of the dilating finger. On the other hand, the valve which is not calcified, not greatly indurated, but merely closed at its orifice as though by a draw string will usually tear across the thinner anterior lip. Thus, a patient ideal for simple lateral commissurotomy must die from uncontrollable regurgitation. We have demonstrated this mechanism both in the pathology laboratory with fresh specimens, and also to our sorrow in a living operated patient.[9, 10]

However, the aortic valve in serious acquired clinical stenosis appears to have no exact pathologic counterpart to this "purse-stringed" state. Indeed, the free edge of the cusp in aortic stenosis appears to bear the brunt of the disease process. It is thickened, indurated, and tough. It is often ossified. By simple forceful dilatation of the stenotic aortic valve in the laboratory it is possible to tear open one or more of the sealed commissures without injury to the valve cusp itself. Such an opening of the valve should produce little if any additional regurgitation, since the cusp as a whole will function better after mobilization. True, it would be unusual for all three commissures to tear open with restoration of essentially normal valve function. However, the powerful hypertrophied left ventricle, able as it is to compensate until veritably only a trickle of blood can pass the aortic barrier, will readily respond to even moderate relief of the obstruction.

We have therefore devised an instrument shaped like a large pencil with a blunt point. This is inserted through an incision in the neck into the lumen of the right common carotid artery. It is gently guided through the innominate artery into the ascending aorta, and soon impinges upon the aortic valve. This is readily recognized both by resistance to further passage and by the direct



A.

B.

Fig. 24.—*A*, Aortic dilator with single dilating arm. *B*, Aortic dilator with triple dilating mechanism.

transmission of the cardiac movements to the operator's hand through the instrument. The instrument is then withdrawn about two centimeters, redirected slightly, and propelled forward with fingertip touch. After a number of such attempts the instrument will engage within the narrowed valvular orifice and can then be inserted well into the ventricle. This location is recognized by even more vigorous transmitted cardiac pulsations, and also by an increase in the systolic thrill transmitted to the operator's hand via the instrument (Figs. 24 and 25).

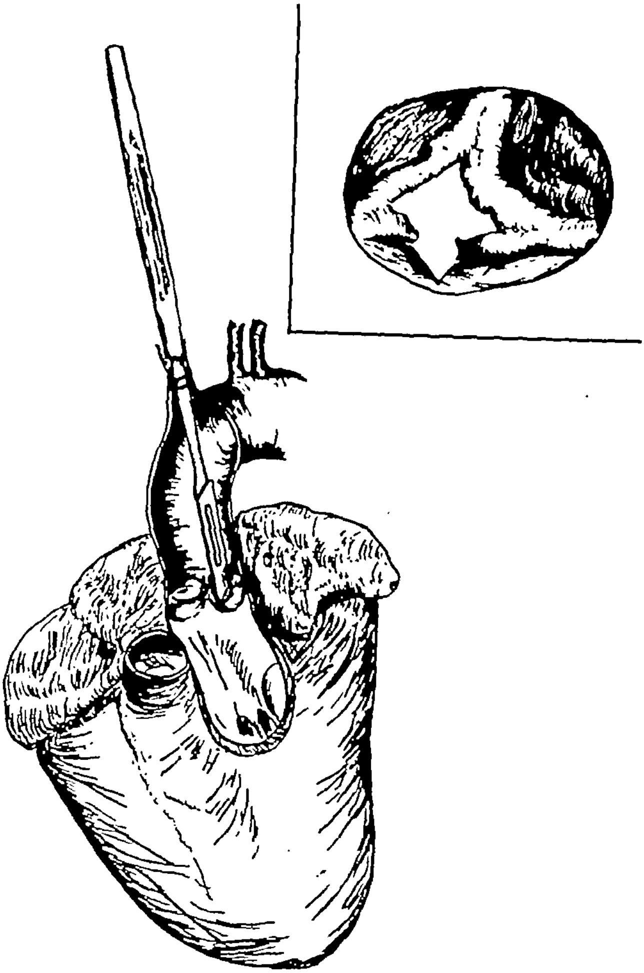


Fig. 25.—Dilatation of stenotic aortic valve. Inset shows hoped for separation of all three fused commissures.

The dilating mechanism is then gently opened by a turnscrew on the handle of the instrument, gradually dilating the narrowed orifice to or past the point of commissural separation. Blood flow through the aortic orifice is maintained by a lack of continuity of the dilating surface. After sufficient dilatation is deemed to have been accomplished the instrument is closed and removed. The carotid incision is repaired by a continuous suture of arterial silk.

We have performed this operation upon two persons with multivalvular lesions, one of which was severe aortic stenosis. The details of these operative cases will be presented elsewhere. Both patients withstood the procedure well. Both presented postoperative objective evidence of enlargement of the aortic valve orifice, and both appeared clinically improved. Neither, by virtue of associated myocardial disease and of coexistent mitral regurgitation, was considered suitable for major thoracotomy and direct attack upon the heart. Both patients are recently postoperative and have not reached a point at which significant conclusions can be drawn regarding the permanence of the effects of valvular dilatation. It is even conceivable that repeated dilatations might be necessary after the elapse of time. There is no anatomical or surgical reason why repetition of the procedure should not be feasible.

SUMMARY AND CONCLUSIONS

1. Our entire experience with attempts to devise a reasonable surgical method for correcting or alleviating aortic stenosis has been presented.

2. Direct valve grafts and vein-valve grafts have been attempted without significant success.

3. Artificial valves have not been used, feeling that insertion of such valves beyond the orifices of the coronary arteries might well be unphysiological. When employed to replace the diseased aortic valve anatomically, such valves may be acceptable.

4. Attempts to by-pass the stenotic aortic valve by double aortic grafts incorporating intact aortic valves have been made. These grafts have anastomosed the aorta to the left ventricular chamber, both directly through the ventricular wall and via the left auricle and mitral route. For technical, physiological, and other reasons, these grafts may well be inapplicable in human aortic disease.

5. The procedures of Smithy and Parker have been duplicated. It is felt that the wide division of an aortic valve by either punch excision or simple incision produces regurgitation of greater magnitude than can be tolerated by diseased human hearts. The enormous hypertrophy of the left ventricle in aortic stenosis with its diminutive lumenal chamber effectively mitigates against prompt and adequate dilatation of this chamber, so essential for proper compensation in sudden, surgically produced aortic regurgitation.

6. A clinical attempt to divide a fused aortic valve into a bicuspid valve similar to the Brock procedure for congenital pulmonary valvular stenosis produced unexpected regurgitation and terminated fatally.

7. It seems probable that division of the fused valve commissures is desirable. This has not been accomplished as yet, either digitally or under direct cardioscopic vision.

8. Since the pathology of aortic stenosis lends itself more favorably to mechanical dilatation than does mitral stenosis, a method of dilatation has been developed. The relative ease with which dilatation can be accomplished retrogradely through the right carotid artery and ascending aorta has led us to abandon the more hazardous ventricular approach for the present.

9. Two patients with aortic stenosis have recently been submitted to mechanical dilatation using the cervical approach, with early clinical improvement.

ADDENDUM

Since submission of this manuscript for publication we have repeated the described technique in one case. Unfortunately a false passage was produced because of difficulty in entering the stenotic valve from above. This resulted fatally. Since then we have returned to the ventricular approach and have successfully dilated one stenotic aortic valve by that route.

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DISCUSSION

DR. A. E. BLOOMBERG, New York.—Dr. Bailey and his associates have presented an extremely interesting paper. As he pointed out, and recent writings of Dr. Blalock, Dr. Harkins, and others have attested, the full surgical attack upon the heart must await methods of visualizing within the heart. Such cardioscopes as have been made have relied on contact methods or utilized displacement chambers through which operation was not feasible. It occurred to me some time ago that a stream of fluid directed under great pressure against an object might displace the blood and might permit operation through such displaced blood. To that end we had several instruments made, and I shall discuss the latest one.

(Slide.) This shows the assembled cardioscope; the scissors at the end of the instrument is actuated by a rod at the end of the instrument; this makes for great cutting strength.

(Slide.) The fluid enters at this inlet and runs down a channel around the telescope. The next slide shows the instrument in cross section.

(Slide.) We have been able to visualize all the cardiac chambers and all the valves of the heart, approaching them through the auricles, the ventricles and, in the case of the aortic valve, the innominate artery. The valves move so rapidly that only a momentary view is afforded. However, when the approach is through the ventricle we have been able to pick up a papillary muscle or corda tendinea on the end of the scissors or hook, using another instrument we have, and follow it up to the valve, fixing the valve for a slightly longer period of time. In an attempt to fix the valve and simulate stenosis to some extent, we have opened the right auricle and sutured the tricuspid cusps together. Following closure of the auricular incision we have inserted the instrument through the right auricular appendage; it is then much simpler to visualize the valve and we have been able to cut the valve in several instances, although this instrument also has a defect in that the best focal point falls between the end of the telescope and the cutting scissors, but we feel we will be able to change that without too much difficulty.

It takes approximately two and one-half minutes for 500 c.c. of fluid to run through the cardioscope at 100 millimeters of pressure of mercury, but by utilizing short bursts of fluid and by removing blood from the femoral artery we have been able to obtain survivals. Some of our dogs have been operated upon two and three times. The dog seems to stand dislocation of the heart incidentally to the use of a straight instrument well, but this would not be true of human beings. Instruments that have an appropriate curve will be designed.

DR. FRANK S. DOLLEY, Los Angeles.—It is not possible by any statement of mine to detract in the least from the epochal work Dr. Bailey has done in connection with the surgical treatment of the aortic valve. I have no hesitation, therefore, in speaking of a tentative experiment of mine begun a number of years ago. It is of definite interest in connection with this work of Dr. Bailey's.

In 1925, following Graham's and Allen's experiments with their cardioscope, and shortly after Cutler's work on aortic valve division, I had constructed for me by an instrument maker in London a steel fingernail. It was so made as to permit the distal phalanx of my right forefinger to slip snugly into this sleevelike instrument. There was an opening to admit my own fingernail. My this means, control of the steel fingernail could be carefully maintained. Another large palmar aperture left exposed the pad of the distal phalanx, so that orientation could be established and maintained.

The purpose of this steel fingernail was by its use to convert a mitral stenosis to a regurgitation. It was planned to introduce the index finger into the left atrium through the auricular appendage. The exposed pad of my own finger would reach the stenotic valve. By means of the hard steel fingernail immediately distal to my own, with a scissorlike cutting motion it would be possible to divide a valve leaf sufficiently to produce conversion from stenosis to regurgitation. At the proximal rim of the steel sleeve there was a small hole. A strong thread carried through this hole and out to the other hand would prevent the loss of the instrument as the index finger was being withdrawn.

I regret very much that for several reasons I have not yet attempted by this means to convert a mitral stenosis to a livable regurgitation.

THE EXPERIMENTAL CREATION AND CLOSURE OF AURICULAR SEPTAL DEFECTS

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MARVIN E. JOHNSON, M.D. (BY INVITATION), AND (BY INVITATION)
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INASMUCH as the clinical auricular septal defect is a static structural lesion, it would appear to be a type of disease which should be amenable to surgical repair. The malformation is apparently fairly common,[1, 2] and because of gradually progressive changes in hemodynamics, the life span of these patients is usually curtailed. Clinical attempt at closure of this defect has been reported.[3] Lack of data on oxygen saturations in the right auricle before and after the attempted closure, however, make analysis of the effectiveness of the procedure impossible. This paper is a report of our experience with the creation and closure of auricular septal defects in the experimental animal.

THE CREATION OF THE DEFECT

For the purpose of studying methods of closure, it is desirable to create an experimental defect which lies as nearly as possible in the anatomic location of the common clinical lesion. Congenital septal defects occur in two separate areas having different embryologic origins as clearly described by Patten.[4] In the first type, which occurs uncommonly, the defects are due to arrested development of the septum primum and lie in the extreme inferior portion of the septum directly overlying the atrioventricular valves. In the second and by far the more common type, the defects result from arrest in the descent of the septum secundum coupled with abnormally extensive resorption of septum primum. This produces essentially a failure in the development of the superior margin of the foramen ovale and these defects thus extend from approximately midseptum into the upper anterior quadrant. It is with the experimental creation of this second lesion that we are primarily concerned.

Our initial attempts to create a defect were made by inserting a narrow knife blade through the auricular wall and placing an elliptical incision blindly through the septum. We found it was quite possible to make the cut 1 or 2 cm. in length, but these incisions invariably healed rapidly, and three weeks later, inspection of the septa revealed them to have returned to an intact and essentially normal state. Recently, Martin and Essex[5] have reported better success and an occasional lasting defect using this method.

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However, we concluded that it would be necessary to actually remove a segment of the septum if success were to be obtained. The initial approach was by means of a rotary punch applied blindly through the wall of the auricle using a purse-string suture. Because the septum is so flexible and because it is in constant motion, our success with this method was minimal. In one animal we managed to create a ragged defect about 1 cm. in diameter, which had begun to heal over when inspected at two weeks.

A rotating blade around the end of a cardioscope encountered the same difficulties. Although it was possible to identify visually the various landmarks in the auricle and on the septum, and thus the effort was directed more accurately at the proper anatomic area, the results were equally disappointing.

It appeared desirable, therefore, to attempt to create the lesion under direct vision. *Early in 1948, we devised an instrument out of a standard type sponge* forceps with which it was possible to approach the septum with a limited but bloodless field. By bending the blades of the forceps to form a circle one could compress the two walls of the auricle against the septum over an area of 1.5 cm. without embarrassing the action of the heart for periods of from four to as long as thirty minutes. Incision in the right auricular wall brought us directly down to the septum and a defect about 1 cm. in diameter, roughly circular in shape, could be made with the scissors or a small sharp knife. The animals tolerated this procedure well on the whole, but to our disappointment, we found that defects of this size, in spite of the fact that there had been loss of substance, uniformly *tended to heal over spontaneously in a period of four to eight weeks.* For this reason, we abandoned this method.

At about the same time Dodrill[6] in Detroit was developing quite independently a similar instrument. In his subsequent report, the illustrated defects, which originally were even larger than ours, appeared to be healing at one month and looked no bigger than the coronary sinus.

At about this time, August of 1948, Blalock and Hanlon[7] published their ingenious method for the creation of a communication between the auricles. This shunt, however, is placed well posterior and superior on the wall of the right auricle and thus lies behind and above the usual anatomic site of the clinical defect. For our purposes, therefore, this procedure did not appear ideal; but if one desires to establish a permanent auricular shunt for experimental or therapeutic reasons, we believe this is the method of choice.

Accordingly, we turned to an attempt to excise the septum under direct vision with the auricle open and the blood flow temporarily occluded. This is a technique which was used by Templeton and Gibbon[8] in their experiments on the tricuspid valve.

The chest is opened by an intercostal incision in the fourth interspace on the right side. The azygos vein is divided between ligatures near its entrance into the superior vena cava. The superior and inferior venae cavae are onw mobilized and umbilical tapes are passed beneath them to serve as temporary ligatures. The pericardium is opened widely in a vertical direction anterior to the right phrenic nerve, and retracted by silk sutures. Two sutures are placed in the auricular wall to demarcate the ends of the proposed incision which is about 3 cm. in length, running vertically, with the lower end at the point of junction of the inferior vena cava with the auricle and about 1 cm. anterior to the attachment of the pericardium. Two additional retraction sutures are placed about 2 mm. apart, straddling the midpoint of the proposed incision. One assistant now pulls up on the hemostatic umbilical tapes occluding the venae cavae. This is his only responsibility, and he maintains this control throughout the procedure until instructed to release by the operator. The two medial silk retention sutures are held by the first assistant. The operator makes the auricular incision with the scissors and then immediately sucks out the auricle with the sucker. There is a very small amount of blood entering the auricle from the coronary sinus. The landmarks are identified, particularly the coronary sinus. A point in the septum 1 cm. superior and 1 cm. posterior to the coronary sinus is grasped with the sharp arterial forceps, elevated, and excised with the scissors. A roughly circular piece of tissue about 2 cm. in diameter is removed. Surprisingly little blood emerges from the left auricle through this defect. It will be remembered that blood flow through the lesser circuit has been halted during the procedure and since the left auricle is dependent, the force acting to expel blood upward through the septal hole is minimal (Fig. 1).

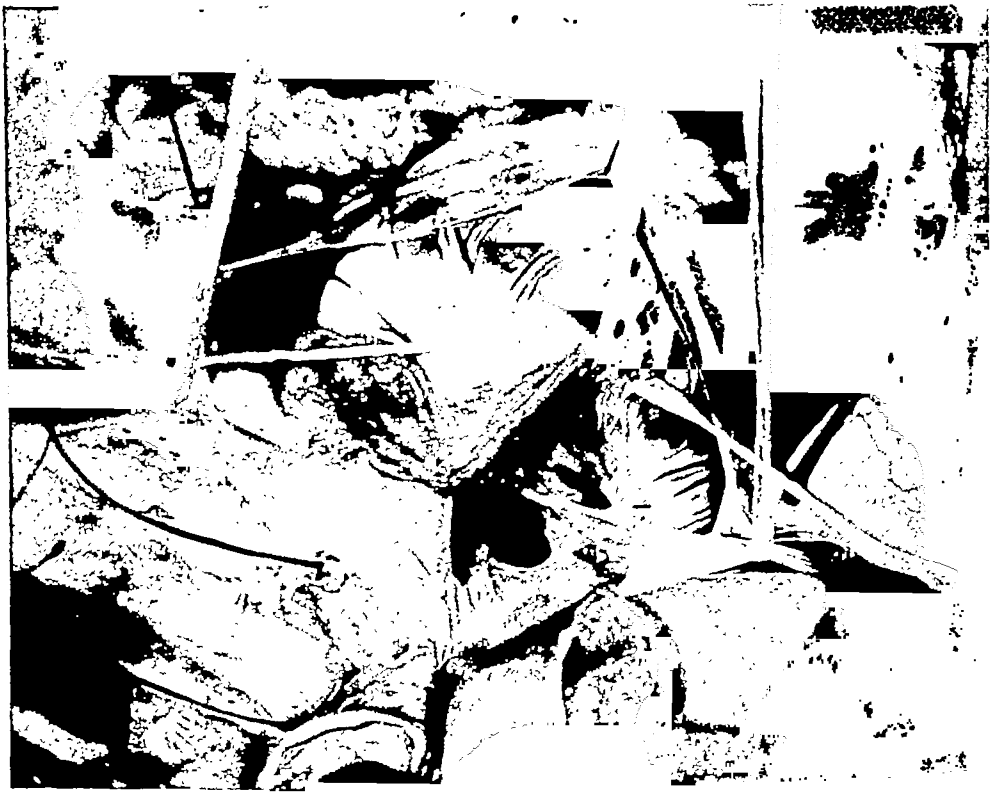

Fig. 1.—Operative view of freshly created auricular septal defect. The venae cavae are temporarily occluded and the wall of the right auricle is open. The defect is superior and posterior to coronary sinus.

The chest cavity is now immediately flooded with saline solution. The operator pulls upward on all four auricular retention sutures controlling the extremities of the incision and the first assistant applies the curved spring clamp. The upward pull on the umbilical tapes is now released, and blood flow from the venae cavae, which has been obstructed between one and two minutes, is at once resumed. The incision in the auricle is now closed at leisure with everting mattress sutures of 000 silk which effects an endocardium-to-endocardium closure. The spring clamp is removed, the pericardium closed, and the chest wound repaired. The animal's recovery is uneventful.

It is remarkable that the disturbance in cardiac rhythm is so slight. In no instance did either auricular or ventricular fibrillation supervene. Neither did any evidence of interference with the sinoauricular pacemaker occur. One pitfall of the operation is the possibility of exceeding the margins of the septum and cutting through the wall of the right auricle. Very accurate placement of the septal excision is essential.

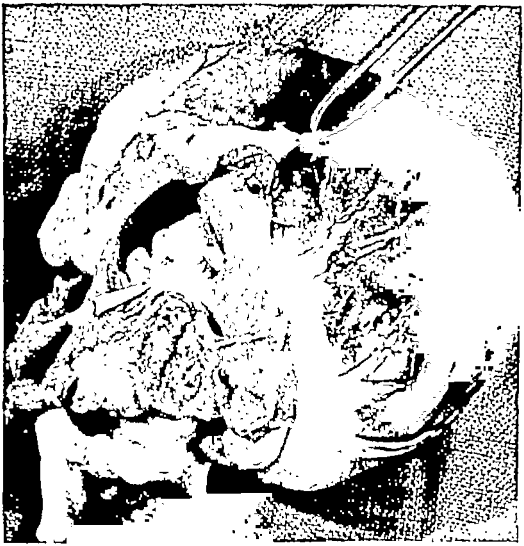

Fig. 2.—View through right auricle of healed septal defect three months after creation. Arrow points to scar in septum; small pledget is in coronary sinus.

We have observed two complications. In one animal death occurred two hours postoperatively. Autopsy revealed air emboli of the left coronary arteries. This is the only animal which had any symptoms of air embolus. In the experience of Martin and Essex with this technique, air embolism was common. It is possible that our method of immediately flooding the chest cavity with saline after the defect was cut was helpful in preventing this complication. In another, upon second operation for the purpose of repairing the defect, a firm intraluminal thrombosis was found in the right auricle adherent to the incision in the auricular wall.

The fate of septal defects created in this fashion is most extraordinary. In spite of the removal of the major portion of the septum, healing commonly occurs in a period of from two to three months, often with complete restoration of a functional septum. It would appear that the auricular septum has great powers to repair a traumatic defect, that careful endocardium-to-endocard coaptation is essential if the defect is to persist (as in the Blalock-Hanlon procedure), and that blind or open surgical incisions or excisions of septum will not consistently remain patent (Fig. 2).

However, for the purposes of experimental closure a preparation was accomplished which simulated the clinical lesion, if closure was attempted within a month of the creation of the defect.

CLOSURE OF THE DEFECT

In 1947, Cohn[9] described an experimental method for the closure of small auricular septal defects in the dog. The lateral wall of the right auricle was pushed against the septum and two sutures were placed to hold it in this position. A wire snare was threaded into the auricle around this portion of wall, and the button-shaped section attached to the septum was cut free, allowing the rest of the wall to revert to normal position. The hole in the auricle left by this maneuver was sutured closed.

This ingenious operation seemed to us to have two potential dangers. During the period of initial invagination of the wall, blood flow from the venae cavae was disturbed and cardiac irregularities were commonly encountered. Second, after excision of the segment of wall, the surface exposed to the internal blood flow in the right auricle was the external surface of the myocardium; it was not lined with a smooth endocardial layer. It seems likely that the factors most suitable for the initiation of intra-auricular thrombosis were thus established. If a method utilizing auricle wall could be devised which did not interfere even temporarily with blood flow and which left exposed to the blood stream only endothelialized surfaces these potential dangers might be eliminated. Such a method is here presented.

The fundamental concept of this technique is to invaginate both auricular appendages and to fasten their tips firmly together through the septal defect. This converts the lumen of the auricle to a hollow space eccentrically "doughnut" in shape, entirely lined with endothelium. No interference with blood flow is encountered. The procedure is as follows:

Under intravenous nembutal anesthesia, using intermittent positive pressure endotracheal oxygen, the animal is placed supine on the operating table and both sides of the chest are prepared and draped. Bilateral anterior intercostal thoracotomies are placed in the fourth interspace, and rib retractors inserted. Eight cubic centimeters of 2 per cent procaine are injected into the pericardium. Attention is first directed to the left side. A T-shaped incision is made in the pericardium over the tip of the left auricle lateral and posterior to the emergence of pulmonary artery. Left auricular tip is identified. A moist drape is now placed over the wound and activity is shifted to the right side. A vertical incision is made in the pericardium the length of the auricle, just anterior to the phrenic nerve. The right auricular tip is seized with the toothed forceps and a purse-string suture of 000 silk is placed at the very apex. The eye end of a standard surgical probe is thrust through the loop into the auricle and the purse string is tightened to effect hemostasis. The bent probe is advanced by feel into the inferior vena cava. It is then drawn slowly upward feeling with the tip along the septum seeking the defect. The coronary sinus may be entered, in which case the probe can be felt in the atrioventricular groove posteriorly. From here the defect lies superior and posterior. If the tricuspid valve is entered, the probe is too far anterior. Usually only one or two tries are sufficient to pass the probe through the defect into the left auricle. Care must be taken that it does not progress out one of the left pulmonary veins. The left incision is now inspected and by feel and direct vision the tip of the probe is manipulated until it lies in the very apex of the left appendage. It is pushed through the muscle at that point (Fig. 3).

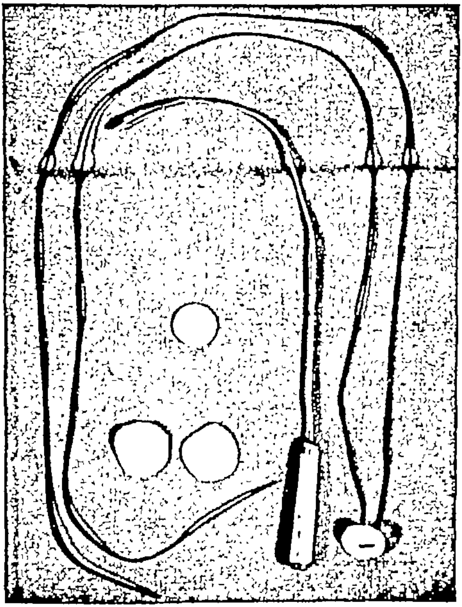

Fig. 3.—A bent surgical probe, two polyethylene buttons, and two pieces of Gelfoam are the only special equipment needed for inversion of the auricular appendages.

The first assistant now rapidly threads the eye of the probe with the two ends of a strand of No. 1 silk on which has previously been threaded a circular button of stiff Polythene, 1½ to 2 cm. in diameter. A piece of Gelfoam lines the inner side of the button. The probe is now entirely withdrawn carrying with it the silk strand. This is pulled up to snug the Gelfoam against the left tip and to start the inversion of the left appendage. A similar piece of Gelfoam and Polythene button is now threaded onto the ends of the silk, the first throw of a surgeon's knot is placed, and the throw gradually but firmly tightened until it is quite snug. This manoeuver inexorably draws the inverted tips of the auricles toward each other until they abut through the septal defect. The two buttons can be identified by feel as having been brought into close apposition in the midline. The knot is finished and the ends cut.

This entire manoeuver can be accomplished with almost no loss of blood, and has not been accompanied by any severe disturbance in cardiac rhythm. The heart does not need to be displaced, and no interference with blood flow is encountered at any time. It remains only to repair the pericardium, expand the lungs, and close the incisions in the usual fashion.

A series of ten dogs with artificially created defects have been closed using this technique. The condensed operative protocols of these animals are seen in Table I.

TABLE I. CONDENSED PROTOCOLS OF CLOSURE OF AURICULAR SEPTAL DEFECT

DOG NUMBER	DATE DEFECT CREATED (1949)	DATE DEFECT CLOSED (1949)	REMARKS
125	March 15	April 8	Killed Jan. 18, 1950. A 2 cm. defect approximately one-half closed by repair. Remainder of defect closed by small organized thrombus
141	April 15	May 11	Sacrificed Sept. 27. An 8 mm. defect was approximately two-thirds closed by repair
145	April 22	May 9	Dog still alive and healthy. Normal ECG, and normal cardiac catheterization
147	April 25	May 25	Sacrificed Dec. 20. A 1 cm. defect was two-thirds closed by repair
148	April 27	May 31	Died 8 hrs. postrepair of bilateral atelectasis. A 6 mm. defect was totally closed by repair
149	May 2	June 1	At second operation, a firm clot felt in right atrium. Dog died June 10, of empyema. The 8 mm. defect was totally closed. An organized thrombosis was found in right atrium
161	June 6	June 28	Sacrificed Dec. 20. A 1 cm. defect was completely closed by repair. Heart appeared normal in size
164	June 8	June 30	Dog still alive and healthy
185	July 8	July 27	Sacrificed Sept. 24. The 9 mm. defect was completely closed by repair
211	Aug. 3	Aug. 25	Dog died on table during skin closure. Cause of death not identified. A 6 mm. defect was well closed by the repair

DISCUSSION

The effect on the cardiovascular hemodynamics of the creation of these septal defects is usually quite minimal within the period of time which they have been observed. The dogs remain quite active and apparently healthy. Occasionally, at second operation the right auricle appears moderately enlarged. The left auricle appears normal.

Cardiac catheterization studies were performed on the animals to evaluate changes in hemodynamics occurring after creation of the defect and after the subsequent repair. An increase of 1.0 volume per cent or more in the oxygen content between the superior vena cava and the right ventricle was chosen as the minimal criteria necessary to suggest flow of oxygenated blood through the septal defect. Table II is a summary of the catheterization studies. It will be seen that in most instances, the status of the auricular septum was accurately reflected by the oxygen saturation studies; but in four animals (Group 3) the

TABLE II. CARDIAC CATHETERIZATION STUDIES

	A. Creation of Defect	
1. Abnormal blood flow; defect proved	No. 125, 145, 147, 148, 161	Catheter revealed status
2. No abnormal blood flow; no defect present	No. 141, 159, 163	
3. No abnormal blood flow; defect proved	No. 117, 149, 185, 211	Catheter failed to reveal status
	B. Repair of Defect	
4. Returned to normal blood flow	No. 125, 145, 147, 161	
5. Did not return to normal flow	None	

catheterization failed to reveal a defect which was subsequently proved to exist. Apparently, at the time of the study, there was no significant left-to-right flow of blood through the defect. It is probable that in the early stage of this abnormality, blood flow may be variable.

What is the functional efficiency of the method of closure? In the four animals which had evidence of abnormal blood flow before repair, catheter studies following repair revealed a return to normal hemodynamics. This data is presented in Table III. We think the evidence is suggestive that abnormal blood flow through the experimental defect is effectively prevented by the operation.

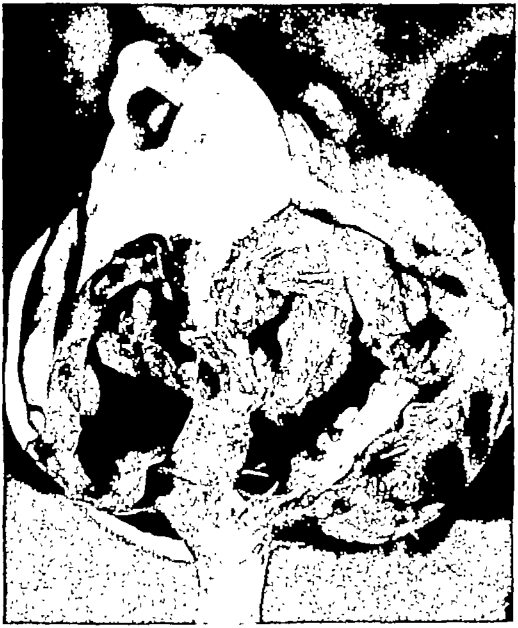

Fig. 4.—*Seen from above, the inverted auricular tips* abut through the septal defect. Autopsy specimen obtained from Dog No. 161, six months following repair, shows smooth endothelial surfaces, lack of thrombosis, and effective closure of defect.

The bilateral thoracotomy was well tolerated by the animals. In only one (No. 148) was atelectasis a significant complication, and it is probable that we were careless in re-expanding the lungs in this animal at the close of the operation.

Intra-auricular thrombosis occurred in only one instance, and this was apparently a result of the creation of the defect rather than of the repair, since it was felt to be present at the second operation. Thrombosis, however, might well occur if auricular rhythm were disordered. This complication did not occur in any of the animals in this series. It is possible that the enlarged, dis-

TABLE III. EFFECT OF CLOSURE OF SEPTAL DEFECT ON CATHETERIZATION FINDINGS (GROUP 4, TABLE I)

	VOL. PER CENT O_2 SATURATION (BEFORE CLOSURE)				VOL. PER CENT O_2 SATURATION (AFTER CLOSURE)				O_2 SAT. DIFF. S.V.C. TO R.V.	
DOG NUMBER	SUPERIOR VENA CAVA	RIGHT AURICLE (1)	RIGHT AURICLE (2)	RIGHT VENTRICLE	SUPERIOR VENA CAVA	RIGHT AURICLE (1)	RIGHT AURICLE (2)	RIGHT VENTRICLE	BEFORE	AFTER
125	8.5	8.1	9.1	11.0	10.5	10.5	10.3	11.0	1.5	.5
145	7.3	8.0	7.3	8.9	10.3	9.8	10.8	9.7	1.6	-.6
147	9.5	11.2	10.9	11.2	9.3	8.0	8.3	9.3	1.7	0
161	7.1	7.0	8.0	8.8	12.0	11.6	12.2	12.2	1.7	.2

tended auricles of the clinical patient would not react so kindly to this manipulation as did the auricles of these essentially normal dogs.

There was no evidence of any interference with blood flow or with auricular function by the inverted auricular tips. This is apparently because anatomically the inversion occurs in the upper anterior quadrant of the lumen of the auricle, while the blood flow occurs primarily in the posterior and inferior quadrants. In addition, the intraluminal auricular pressure apparently compresses the inverted appendage so that its diameter, as it traverses the auricle, is usually quite small, much less than the size of the button at its tip (Fig. 4).

In some of the specimens, the edge of the defect had healed firmly to the auricular appendage passing through it either totally or in part. It is possible that this is related to the traumatic origin of the defect and would not occur in defects which were congenital.

SUMMARY

1. A method for the creation under direct vision of an auricular septal defect in dogs, which simulates anatomically the congenital clinical defect, is described.

2. These defects have a strong tendency to spontaneous closure by healing.

3. An operation for the anatomical and functional obliteration of these experimental defects by inversion of the auricular appendages has been devised which is well tolerated by the animals.

4. The effectiveness of this procedure in reverting abnormal blood flow to normal is suggested by cardiac catheterization studies.

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DISCUSSION

DR. F. D. DODRILL, Detroit.—I rise to comment on a few points about atrial septal defects with which we have had some experimental and clinical observation. Some of you will recall that last year I showed a method by which we could excise the major portion of the atrial septum under direct vision and at the same time close it by a method of suture. We have tried leaving these atrial defects open and found, as Dr. Swan did, that they nearly all close in a matter of a few months. Moreover, it has been our experience that we could not simulate the hemodynamics of the disease in the human being. That, of course, is primarily the reason why the defects close in the experimental animal, because the blood flow is not sufficiently great to maintain its patency. It would be nice if all atrial defects in the human being were in a position in the center of the septum. It is difficult, indeed, to get an accurate idea as to where the majority of them are, from the pathologic literature. There are directly contradictory reports; some will say they are in the so-called center of the septum, and others report that the majority are in the inferior portion of the septum which does not correspond to the hole which we create in the center. It has been our experience in the few cases that we have explored, that the atrial defect has been directly in continuity with the bicuspid and the mitral valves. It is therefore a sort of half-moon defect, the lower and inferior portion of the circle being the valves themselves.

It would seem to me that the type of defect would not be so amenable to the type of closure which Dr. Swan has shown, because of the interference with ventricular filling.

DR. SANFORD E. LEEDS, San Francisco.—I would like to discuss one point regarding the persistence of artificial septal defects. As you know, there are several methods of producing septal defects, and I think the method we use is inferior to the visual methods Dr. Swan and Dr. Dodrill have mentioned today. We use a modified nasal septal punch of the Yankauer type, and the main advantages are that the method is extremely simple and there is no trauma to the right auricle. We had one animal in which the defect had persisted for 162 days at the time it was sacrificed, and apparently the defect was not closing any further at that time. Why this one persisted I do not know.

(Slides.) The modification of the septum punch consists of a perforated sheet of metal which is soldered over the punch in order to retain the removed portion of the interauricular septum. The left auricular appendage is opened and the septum punch is inserted. The left forefinger is used to palpate the location of the septum between the superior and inferior cavae. It is possible to locate the exact position where the opening is to be made, and then a bite is taken, pressing down on the left forefinger with the punch. It might appear that one would go through both layers and open the outer wall of the right auricle, but this did not occur.

(Slide.) This colored photograph shows the left side of the heart opened with the persistent septal defect which stayed open five and one-half months. Here you see the right side of the septum with the persistent opening which measured 1.4 cm. in diameter.

DR. SWAN (closing).—I would like to thank Dr. Dodrill and Dr. Leeds for their comments. The septal defect which occurs just above the valves, also embryologically carefully described by Patton, is the result of failure of complete descent of the septum primum, and is a very definite clinical entity as Dr. Dodrill stated. The incidence of the various types has not been well worked out. I would agree entirely that it may be impossible in clinical patients to predict preoperatively which type of lesion is present.

A PHYSIOLOGIC EVALUATION OF VAGUS SECTION FOR BRONCHIAL ASTHMA

Karl P. Klassen, M.D., Douglas R. Morton, M.D. (by invitation), and
George M. Curtis, M.D.
Columbus, Ohio

BRONCHIAL asthma has been considered an expression of tissue hypersensitiveness. Certain instances, however, are regarded as something more than resulting entirely from a single process such as allergy, infection, psychoneurosis, or irritation of the mucous membranes of the upper respiratory tract. Various surgical procedures have been postulated, planned, and accomplished on the extrinsic pulmonary nerves in attempts to relieve "intractable" bronchial asthma. Of these, unilateral cervical sympathectomy, stellate ganglionectomy, bilateral cervical sympathectomy, unilateral cervicodorsal sympathectomy, and bilateral resection of the posterior pulmonary plexus have gained some application. The results, in general, are still debatable, yet in certain instances brilliant success has been reported. This has stimulated continued effort toward a surgical approach.

We have reported our studies on the neurophysiology of the tracheobronchial tree. In these a review of the literature pertinent to the anatomy of the extrinsic pulmonary nerves was presented.[1-4] In brief, the bronchi receive a dual nerve supply, derived from the upper thoracic sympathetic and vagus nerves. These nerves meet at the level of the pulmonary hilus to form the anterior and posterior pulmonary plexus, where they are stated to intermingle freely with a partial crossing of some of the fibers to the opposite lung. The sympathetic efferent fibers, whose cell bodies are located in the first four thoracic spinal ganglia, communicate with the sympathetic chain through the upper three white rami communicantes. The sympathetic efferent fibers arise from nerve cells in the intermediolateral cell column of the spinal cord and traverse the upper four thoracic white communicating rami to reach the sympathetic chain. There is evidence that a majority of these fibers pass to the stellate ganglion, where a synapse is made with the postganglionic fibers to the lung. The vagal afferent fibers, whose cells of origin are bipolar and located in the nodose ganglia, are distributed peripherally to the tracheobronchial tree, and centrally to the nucleus of the tractus solitarius. The vagal efferent fibers arise from cells in the dorsal motor nucleus of the vagus and are distributed peripherally to the tracheobronchial tree where they synapse with dendrites of nerve cells from which originate the postganglionic fibers.

Physiologic studies have demonstrated that vagus stimulation and parasympathomimetic drugs cause bronchoconstriction, whereas sympathetic stimu-

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lation and sympathomimetic drugs produce bronchodilatation. In this regard, the work of Dixon and Brodie,[5] and Dixon and Ranson[6] is of importance, inasmuch as they established a physiologic basis for the attempted relief of asthmatics by surgical means. By measuring the fluctuating volume of the right middle lobe of a cat's lung they demonstrated that vagal stimulation consistently produced bronchoconstriction, whereas stimulation of the upper three thoracic sympathetic ganglia or the stellate ganglion resulted in bronchodilatation. The existence of bronchodilator fibers in the vagus nerve and the presence of bronchoconstrictor fibers in the sympathetics was occasionally observed; however, this was considered unusual and insignificant. Partial crossing of sympathetic and vagal fibers to the opposite lung was usually demonstrable. In addition they observed that stimulation of the central end of the cut vagus nerve, after both vagus trunks had been sectioned, produced reflex bronchodilatation. By repeated transections of the nerve tracts, they concluded that the reflex pathway traversed the vagal afferent fibers to the medulla, passed from the medulla to the lateral columns of the cervical cord, and then was carried through the first, second, and third thoracic white communicating rami to the sympathetic chain, to the stellate ganglion, and on through the "accelerator nerve" to the bronchi. Likewise, *they noted that reflex bronchoconstriction could be readily obtained* by stimulating the central end of various afferent nerves such as the sciatic, crural, trigeminal, glossopharyngeal, and vagus, but in no instance was reflex bronchoconstriction found after bilateral section of the vagus trunks. The probability of a higher distribution of these nervous pathways was suggested by the bronchoscopic observations that the presence of bronchoconstriction or bronchodilatation is determined in part by emotional factors. Faulkner[7] observed that thoughts of insecurity and frustration resulted in bronchoconstriction, whereas thoughts of a pleasant and desirable nature produced bronchodilatation.

That the bronchi normally constrict during the expiratory phase and dilate during the inspiratory phase of respiration is a well-known phenomenon. In this regard Ellis has satisfactorily demonstrated that the rhythmic movements of the bronchi are passive and entirely due to the movements of the thoracic wall.[8] We are in agreement with this conclusion in that we have been unable to observe any bronchial movements during thoracotomy, that is, after the negative pleural pressure has been released.

In 1930, Kountz and Koenig[9] reported that vagal stimulation apparently increased the secretion per unit area of bronchial mucosa in the dog, whereas stimulation of the cervical sympathetics caused little change, or possibly a slight decrease in the amount of secretion. Subsequently, Florey and associates[10] demonstrated that stimulation of the peripheral end of the cut vagus and inferior laryngeal nerves in the cat increased the amount of tracheal secretion. The effect was abolished by the administration of atropine. Stimulation of the central ends of the vagus nerve caused the tracheal glands to secrete reflexly when one of the vagus nerves remained intact. In addition, we have observed during bronchoscopy that the administration of parasympathomimetic drugs results in bronchorrhea. That sympathetic stimulation may cause vasoconstriction of bronchial vessels is suggested by the bronchoscopic observation of the blanching of bronchial mucosa by the subcutaneous or topical application of adrenalin.

On the basis of these studies and the findings of many other observers, Alexander[11] presented the following table pertaining to the neurophysiology of the bronchial tree:

Bronchial	*Sympathetic stimulation*	*Vagal stimulation*
Muscles	Relaxation	Contraction
Glands	Inhibition	Secretion
Vessels	Constriction	Dilatation

In order to apply the known neurophysiology of the bronchi correctly in the surgical treatment of intractable bronchial asthma, it is necessary to consider the pathologic physiology of this condition. Most investigators believe that the characteristic wheezing, dyspnea, and prolonged expiration of asthma are due to a narrowing of the bronchial lumen. Inasmuch as the larger bronchi are supported by cartilaginous rings, it is reasonable to assume that relatively the greatest obstruction occurs in the smaller bronchi. Although the exact mechanism responsible for the decreased bronchial caliber has been the subject of considerable debate, two leading theories have received wide acceptance: (1) spasm of the bronchial muscle, and (2) edema of the bronchial walls with excessive secretion of mucus. There is considerable evidence to substantiate each theory; however, Alexander[12] stated: "It is probable that since vagus stimulation, which is the nerve impulse that initiates an attack, causes all three lesions, no one, but all, play a role. In the earlier stages of the disease, edema and bronchial constriction are probably the most important factors, since the mucous glands are small and the production of mucus scant. In long standing asthma increased, thick, tenacious mucus is probably the most important factor in bronchial obstruction."

Unfortunately pathologic confirmation is limited in that relatively few asthmatics die of the disease, and it is difficult to apply the findings of microscopic sections to a functional disturbance. The lack of uniformity of the findings of the few post-mortem examinations on asthmatics is probably due to the variable duration of the disease, the fact that some patients died during a paroxysm while others died of intercurrent disease and the presence of complications, such as pneumonia, heart disease, and emphysema. However, sufficient correlating data are available to permit of certain general statements. Grossly the lungs are usually emphysematous, associated with small intervening areas of atelectasis; the bronchi contain a thick, tenacious sputum which may partially obstruct the lumina; the bronchial walls are thickened, and the bronchial mucosa is usually hyperemic and thrown into folds. In patients dying during a paroxysm constriction of the medium-sized bronchi of 5 mm. in diameter has been reported, whereas the more distal bronchi and the alveolar sacs are distended with trapped air. This gives rise to the belief that the primary pathologic physiology of the asthmatic occurs in bronchi of approximately 5 mm. in diameter.

The microscopic pathology of these bronchi includes:

1. Metamorphosis of the normal ciliated cells to goblet cells and, later, metaplasia to pseudostratified squamous epithelium.
2. Excessive mucus within the bronchial lumen.
3. Infolding of the bronchial mucosa which partially obstructs the lumina.
4. Widening of the submucosal layer in some instances to twice its normal size, which is thought to be due to hyperemia and round cell infiltration, especially eosinophils.
5. Hypertrophy of the bronchial smooth musculature.

On the basis of experimental work demonstrating the nervous control of the bronchial tree, many investigators have suggested that an increased number of bronchomotor impulses cause the bronchospasm, excessive bronchial secretion, and edema responsible for the asthmatic paroxysm. According to this hypothesis, interruption of the proper nerve pathways should alleviate the symptomatology of bronchial asthma. Kümmel[13] was the first to report such an operative procedure in 1923. Although he realized the vagus nerve was the main bronchomotor nerve, he excised the superior, middle, and inferior cervical sympathetic ganglia along with a portion of the stellate ganglion on one side. He reported good results in three cases. Subsequently a number of patients in European clinics were subjected to various operative procedures directed toward the unilateral or bilateral excision of the cervical sympathetic chain and the stellate ganglion. In 1924, Kappis[14] transected the right vagus trunk below the recurrent laryngeal nerve with good results. This led to a combined operative procedure in which unilateral vagotomy and unilateral cervical sympathectomy were performed. Later Kümmel[15] advocated section of the posterior pulmonary rami inasmuch as Bräucher[16] had demonstrated that both sympathetic and vagus fibers supplied the posterior pulmonary plexus and only at this point could complete denervation of a lung be accomplished.

Phillips and Scott[17] in 1929, reviewed over 300 cases collected from the literature of patients with asthma who had received surgical treatment. Unfortunately, many cases had been reported before sufficient time had elapsed postoperatively to allow of critical evaluation. Of those considered eligible for analysis 30 per cent were believed to be "cured," 18 per cent improved, and 45 per cent were unimproved. In 1938, Rienhoff and Gay[18] reported on 16 patients in whom bilateral resection of the posterior pulmonary plexus had been performed. In 1942, further observations were submitted by these investigators[19] in 21 patients, 8 of whom received 50 to 100 per cent relief, and 13 of whom were considered failures.

More recently Miscall and Rovenstine[20] have reported on the value of Novocain block of the stellate and upper four thoracic sympathetic ganglia as a diagnostic procedure in determining the role the sympathetics play in asthma. In all patients successfully blocked, immediate improvement was noted in 78 per cent. The patients responding to Novocain block were considered to be the candidates most likely to receive permanent relief from excision of the right stellate and upper thoracic ganglia. In 21 patients subjected to unilateral cervicodorsal sympathectomy complete relief of asthma was obtained as long as two years subsequent to surgery at the time of the report.

It thus becomes evident that surgical procedures directed toward either the vagus or sympathetic nerves have been reported as yielding good results. Although the rationale for vagotomy is more clear it is difficult to comprehend how sympathectomy could be equally successful, inasmuch as the vagus is considered to be the "bronchomotor nerve." Theoretically, if sympathetic-parasympathetic antagonism exists, sectioning of the sympathetic supply to the bronchial tree should result in unopposed bronchospasm, thus producing an exacerbation of the asthmatic state. That such may occur is demonstrated by the work of Miscall and Rovenstine, in which they caution that Novocain block of the cervicodorsal sympathetics may precipitate status asthmaticus.

In an attempt to explain the good results following unilateral and bilateral cervical sympathectomy investigators have offered the following theories:

1. Bronchial asthma in some instances is due to a reflex mechanism initiated by irritation of the tracheobronchial tree. This gives rise to nerve impulses which traverse sympathetic afferent fibers to the medulla where connection is made with vagal efferent bronchoconstricting fibers. Hence, sympathectomy interrupts the reflex arc on the afferent side.
2. The sympathetic nerves to the tracheobronchial tree contain some bronchoconstricting fibers, as demonstrated by the work of Dixon and Ranson,[6] Binger and associates,[21] and Hebb.[22] Sympathectomy theoretically diminishes the number of bronchomotor impulses, thus decreasing the degree of bronchospasm, secretion, and edema.
3. Co Tui and associates[23] demonstrated that the bronchi were more sensitive to adrenalin following cervicodorsal sympathectomy. Theoretically the small amount of circulating adrenalin in sympathectomized patients may be sufficient to inhibit bronchospasm, thus diverting the asthmatic paroxysm.

Little basis for the first theory is afforded by the findings of our previous studies.[2, 3] Two afferent functions of the bronchial tree were shown to be carried in the majority of patients by the homolateral vagus nerve. In brief this was demonstrated by the bronchoscopic observation that electric stimulation of the nonanesthetized tracheobronchial mucosa resulted not only in paroxysmal cough, but also in pain referred to the anterior chest wall or cervical region. These studies were repeated in patients in whom unilateral vagotomy had been performed below the origin of the recurrent laryngeal nerve. (This latter procedure was performed in an attempt at palliation of patients found to have inoperable bronchiogenic carcinoma at the time of exploratory thoracotomy.) In contrast to the previous observation, electric stimulation of the homolateral nonanesthetized main bronchus failed to elicit cough or pain in all but three patients. These results not only suggest that the afferent fibers which transmit pain from the bronchial tree but also the afferent fibers transmitting bronchial impulses resulting in initiation of the cough reflex are carried by the homolateral vagus nerve. The findings in the three patients found to have pain of homolateral bronchial origin following unilateral vagotomy suggest that the afferent nerve supply of the bronchial tree is derived in part from the contralateral vagus nerve. In these investigations there was no physiologic evidence that the sympathetic system supplies afferent fibers to the bronchial mucosa. If bronchial asthma is due to a reflex mechanism initiated by irritation of the bronchial mucosa, and if interruption of the afferent side of the reflex arc is the desired effect, then from the preceding observations it would appear that vagotomy should be the procedure of choice.

Although there is evidence that bronchoconstricting fibers are carried in the sympathetic system, the preponderance of experimental data indicates that the vagus is the main bronchomotor nerve. Therefore, according to the second hypothesis, if the desired effect in the surgical treatment of asthma is to decrease the number of bronchomotor impulses, again vagotomy would seem to be the procedure of choice.

It is difficult to conceive how unilateral interruption of either the vagus or sympathetic system could be any more than partially successful in that the pathologic physiology of asthma is a bilateral phenomenon. In addition anatomic and physiologic investigations have demonstrated that each side of the bronchial tree receives nerve fibers from the contralateral vagus and sympathetic nerves. Therefore any unilateral procedure would not completely interrupt that particular nervous supply to the homolateral bronchial tree. In this regard the work of Rienhoff and Gay[18] is more logical in that complete denervation of the bronchial tree was performed by bilateral resection of the posterior pulmonary plexus. Although we are in agreement with the performance of a *bilateral procedure, we believe that the sympathetic system should be left intact.* If the theory of sympathetic-parasympathetic antagonism is correct it appears from the foregoing data and discussion that bilateral vagotomy, leaving the bronchodilating sympathetic fibers intact and unopposed, would be the logical operative procedure. From an anatomic and physiologic standpoint to achieve complete parasympathectomy of the bronchial tree, leaving the sympathetic nerves intact, the surgical procedure should consist of a bilateral transection of the vagus nerves above the origin of all branches of the pulmonary plexus.

In previous studies we have demonstrated that unilateral section of the vagus nerve immediately below the origin of the recurrent laryngeal nerve could be performed without any adverse sequelae. There appeared to be no contraindication in the bilateral performance of this procedure. On the basis of this concept our medical colleagues were consulted for approval in the application of this procedure to patients with intractable bronchial asthma who had received all known forms of specific and nonspecific therapy without relief. The protocols of three such cases are herewith presented.

CASE REPORTS

CASE 1.—D. T., No. 491774A, a white girl, 12 years of age, was admitted to the University Hospital on March 2, 1949, with a diagnosis of bronchial asthma. The family history revealed that her younger sister, paternal uncle, and maternal aunt had "hay fever." She began having asthma at the age of 5 years, shortly following tonsillectomy. Initially the attacks occurred more frequently during the summer and fall seasons, and were relieved by adrenalin and aminophyllin.

Six years prior to admission she noted a chronic cough, productive of a grayish-white, thick sputum, and three years later she was found sensitive to ragweed, eggs, and roses. Desensitization was attempted without relief. Her asthmatic attacks had so increased in severity and frequency that she was unable to attend school. During the past two years she had received the usual antibiotics, bronchodilator drugs, and antihistaminics without much relief. Change of climate was transiently effective. During this period sputum became mucopurulent and foul. She was referred to the Research Surgical Service by the allergist for consideration of surgery.

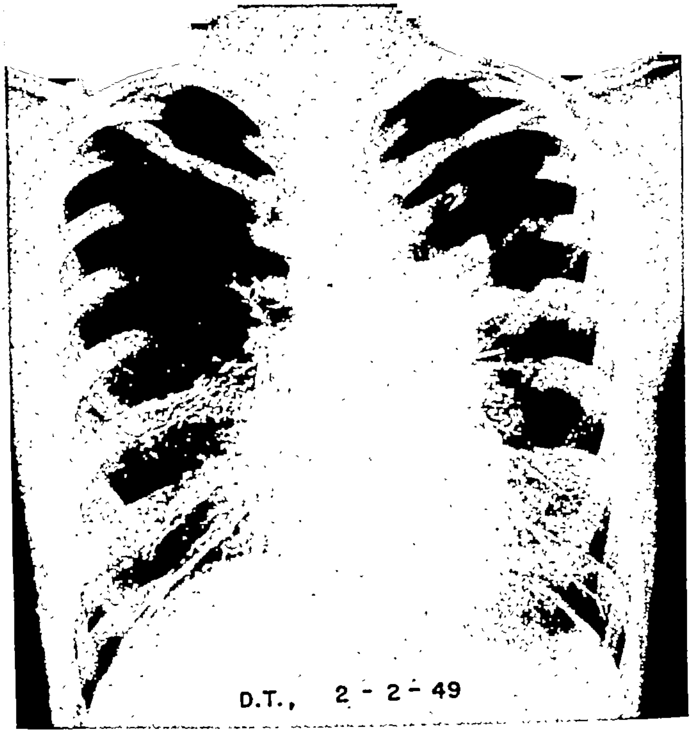


Fig. 1 (Case 1. D. T.).—Preoperative bronchogram revealing right middle lobe bronchiectasis and generalized bronchospasm of moderately severe asthma.

On physical examination her posture was drooping, the shoulders were rounded, the clavicles were raised anteriorly, and the anteroposterior diameter of the chest was increased. The sternum was prominent. There was a dorsal kyphosis. The percussion note was hyperresonant, and expiration was prolonged. Musical râles and rhonchi were heard through both lung fields. Admission white blood count was 10,500 with 5 per cent eosinophils. An electrocardiogram revealed a sinus tachycardia of 165 and right axis deviation. X-ray examination revealed the lung fields to be wide superiorly and emphysematous. A bronchogram demonstrated bronchiectasis of the right middle lobe and generalized bronchospasm (Fig. 1). The vital capacity was 1,700 c.c.

On March 7, 1949, a right posterolateral thoracotomy was performed. Continuous electrocardiographic tracings were made during the surgical procedure. Shortly after induction with Pentothal Sodium (R) endotracheal cyclopropane-oxygen anesthesia multiple extrasystoles were noted on the electrocardiogram. Upon substitution of nitrous oxide, ether and oxygen anesthesia, these changes disappeared. Exploration revealed that the lung tissue was emphysematous and the marginal veins were distended. The right middle lobe was found to be atelectatic and somewhat indurated. The right middle lobe bronchus was surrounded by enlarged lymph nodes. A right middle lobectomy was performed by the individual ligation technique, and the right vagus trunk was transected just below the origin of the recurrent laryngeal nerve. During manipulation and transection of the vagus nerve, no obvious effects

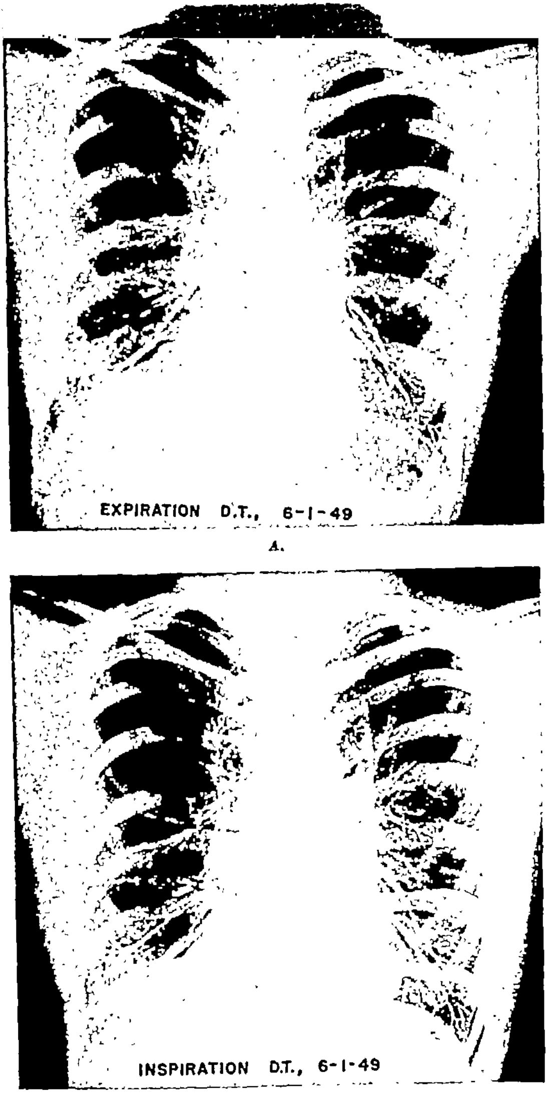


Fig. 3 (Case 1, D. T.).—Bronchograms obtained during expiration (*A*) and inspiration (*B*) following right vagotomy and right middle lobectomy. Comparison of the two exposures demonstrates *the normal occurrence of* bronchoconstriction during expiration and bronchodilatation during inspiration. Note that the same degree of generalized bronchospasm is present during both phases of respiration, and is as marked on the denervated right side as on the left.

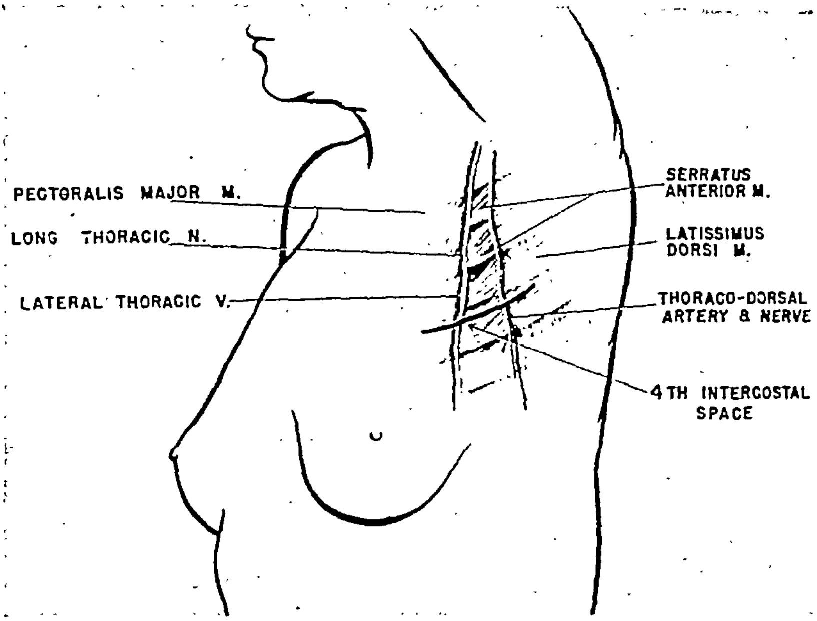


Fig. 3.—Diagram illustrating the lateral surgical approach to the vagus nerve.

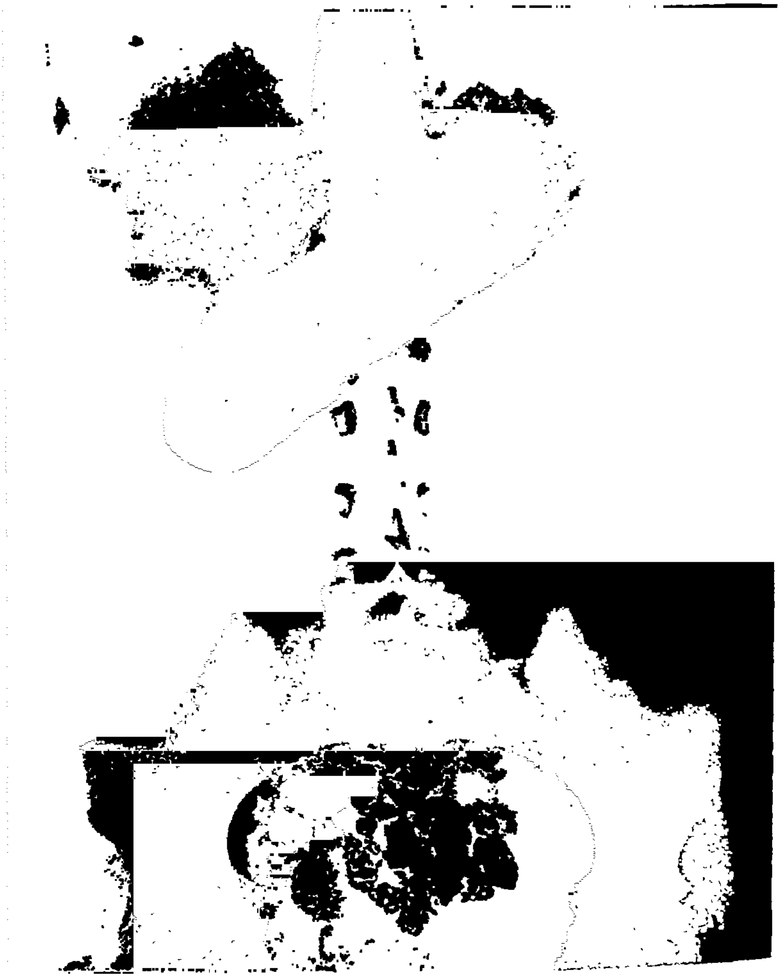


Fig. 4 (Case 1. D. T.).—Roentgenogram revealing 90 per cent gastric retention six hours after the ingestion of barium.

were observed on the electrocardiographic tracings. She was discharged on the twelfth hospital day free of asthma.

Although she remained asymptomatic for three months, a bronchogram performed on June 1, 1949, revealed that bronchospasm was still present (Fig. 2, *A* and *B*). Shortly thereafter a family quarrel precipitated one of the most severe attacks that she had experienced. Following confinement to bed for three weeks she was readmitted to the hospital on June 22 in status asthmaticus. She received aerosol and systemic antibiotics, bronchodilator drugs, and chemotherapy without relief. Aminophyllin suppositories were found to be temporarily beneficial and the patient was discharged somewhat improved. On August 10, she was readmitted during a remission of her illness for consideration of left vagotomy. During an asthmatic attack the left vagus trunk was blocked in the carotid sheath with 1 per cent Novocain without relief. The admission white blood count was 10,400 with 11 per cent eosinophils. The electrocardiogram was interpreted as normal with a rate of 90. The vital capacity was 1,000 c.c.

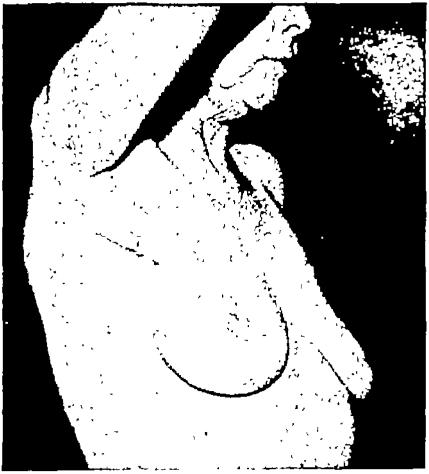


Fig. 5 (Case 2, E. C.).—Postoperative photograph demonstrating the position and extent of the incision on the right lateral approach to the vagus nerve.

On August 24, a left thoracotomy was performed through a 15 cm. incision along the fourth interspace in the midaxillary line (Fig. 3). With the aid of lighted retractors, the vagus trunk was identified and mobilized with a nerve hook at the arch of the aorta. Since *Novocain block of the left vagus trunk had been performed previously without relief, it was* decided that permanent interruption of the remaining vagus nerve was not justifiable. The left vagus nerve was blocked with 1 per cent Novocain immediately below the origin of the recurrent laryngeal nerve without any discernible gross changes in the electrocardiographic tracings. Accordingly, the left vagus trunk was crushed at this point. Postoperatively she did well with the exception of complaints of epigastric fullness and bloating. An upper gastrointestinal series revealed considerable gastric dilatation, lack of peristalsis, and 90 per cent gastric retention of barium at six hours (Fig. 4). Although she remained free of asthma for a period of three weeks, gastrointestinal symptomatology increased in such severity that the administration of Urecholine, 2.5 mg. three times a day, was required. Six months after the second operative procedure, the gastrointestinal symptoms had subsided completely. There was slight but definite decrease in the frequency and severity of the asthmatic attacks. However, she required daily aminophyllin suppositories and an occasional injection of adrenalin.

CASE 2.—E. C., No. 500837A, a 57-year-old white woman, was admitted to the medical service on July 27, 1949, in status asthmaticus. She was cyanotic and comatose. This was her seventh hospital admission for the treatment of asthma.

She first had asthma during childhood; however, the attacks ceased at 12 years of age. She enjoyed relatively good health until five years prior to admission, at which time a

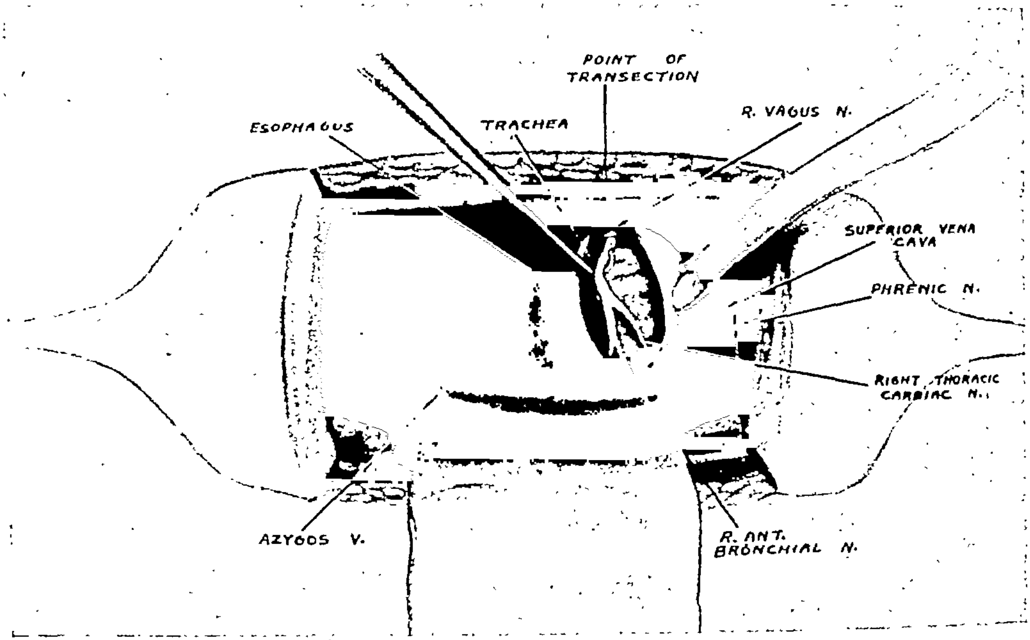


Fig. 6.—Artist's conception of the exposure of the site of transection of the right vagus nerve above the origin of the pulmonary plexus.

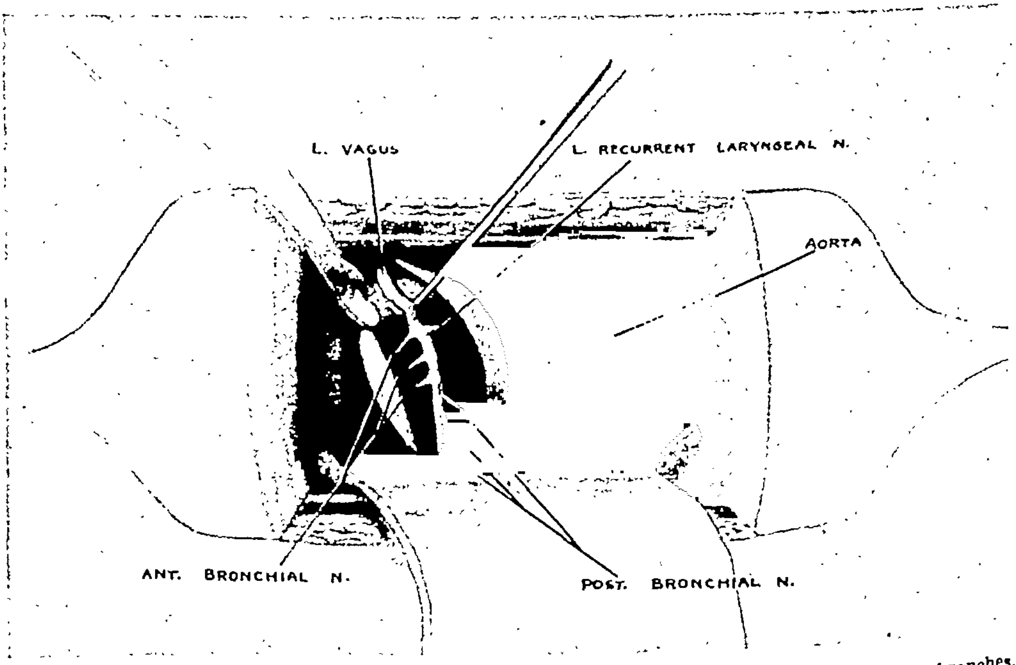


Fig. 7.—Artist's conception of the exposure of the left vagus nerve and its pulmonary branches, all of which were transected.

panhysterectomy was performed. Shortly following this procedure she noted the recurrence of asthmatic attacks characterized by sudden onset of orthopnea, sweating, and wheezing. She had been treated by many physicians. Antibiotics, bronchodilator drugs, and antihistaminics had been employed with only partial relief. Allergy studies elicited a sensitivity to house dust, cat and dog dander. Desensitization was attempted without relief. Despite additional symptomatic therapy the asthmatic attacks occurred in increasing frequency and severity.

During the seventh hospitalization, she remained in status asthmaticus for three days. After interruption of this cycle she continued to have six to eight severe asthmatic paroxysms per day, requiring various therapeutic measures. The frequency and severity of the attacks were such that the patient was afraid to leave the hospital. After forty days of hospitalization the research surgical service was requested to evaluate the patient in regard to surgery. On Sept. 8, 1949, utilizing a lateral approach (Figs. 5 and 6), the right vagus trunk was transected immediately below the recurrent laryngeal nerve. Following this procedure, the patient felt slightly improved. Some members of the staff believed there was less wheezing in the right lung than in the left. Due to the severity of the gastrointestinal symptoms in the first patient (D.T.), on September 28, only the pulmonary branches of the left vagus were sectioned, through a lateral incision (Fig. 7). The vagus trunk was not transected. The postoperative course was benign and she was discharged asymptomatic ten days after the second operative procedure. At monthly intervals examination revealed that she had remained asymptomatic, requiring no medication, and she considered herself "cured." On Feb. 7, 1950, the patient was very cheerful, stated that she felt fine and had gained fourteen pounds in weight. At this time a bilateral bronchogram was performed in order to evaluate the effect of bilateral parasympathectomy on the bronchial tree. Instillation of 8 c.c. of Lipiodol into each side of the bronchial tree precipitated a severe attack of asthma characterized by extreme dyspnea, moderate cyanosis, wheezing, and excessive perspiration. She was treated immediately in the emergency room where 7½ grains of aminophyllin were adminis-

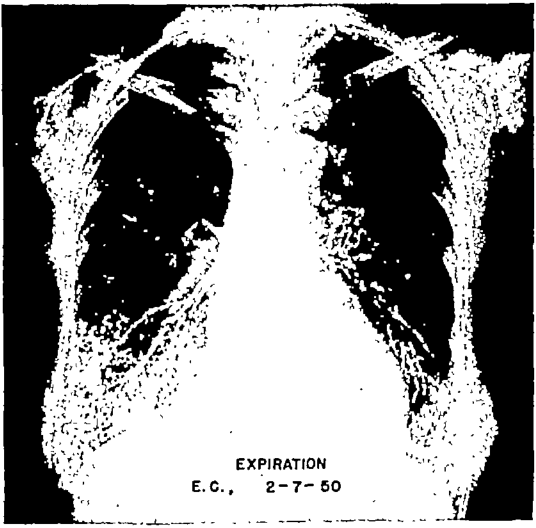


Fig. 8 (Case 2, E. C.).—Bronchogram obtained during expiration after bilateral parasympathectomy of the bronchial tree. Note the persistence of generalized bronchospasm.

tered intravenously and oxygen inhalation instituted. Although she was much improved after one hour, she was hospitalized overnight and discharged the following day. The bronchogram revealed severe spasm of the bronchi (Fig. 8). Since this single episode she has remained free of asthma.

CASE 3.—J. A., No. 492003A, a colored girl, 12 years of age, was first seen in the allergy clinic on Jan. 24, 1945. The following history was obtained: frequent paroxysms of coughing, shortness of breath, and wheezing had begun two years previously. Initially the attacks were more frequent during the fall and damp weather and were often precipitated by the onset of upper respiratory infection. Subsequently the attacks occurred with increasing frequency and severity, unrelated to season or weather. On occasions she noted areas of pruritis on her legs followed by welts. She had had whooping cough, measles, mumps, and chicken pox. There was no family history of allergies. At this time skin tests were negative. The vital capacity was 1,800 c.c. There were several nasal polyps; the nasal mucosa was edematous, and a mucopurulent nasal discharge was persent. The chest was emphysematous, the anteroposterior diameter being increased. Wheezing was heard throughout both lung fields.

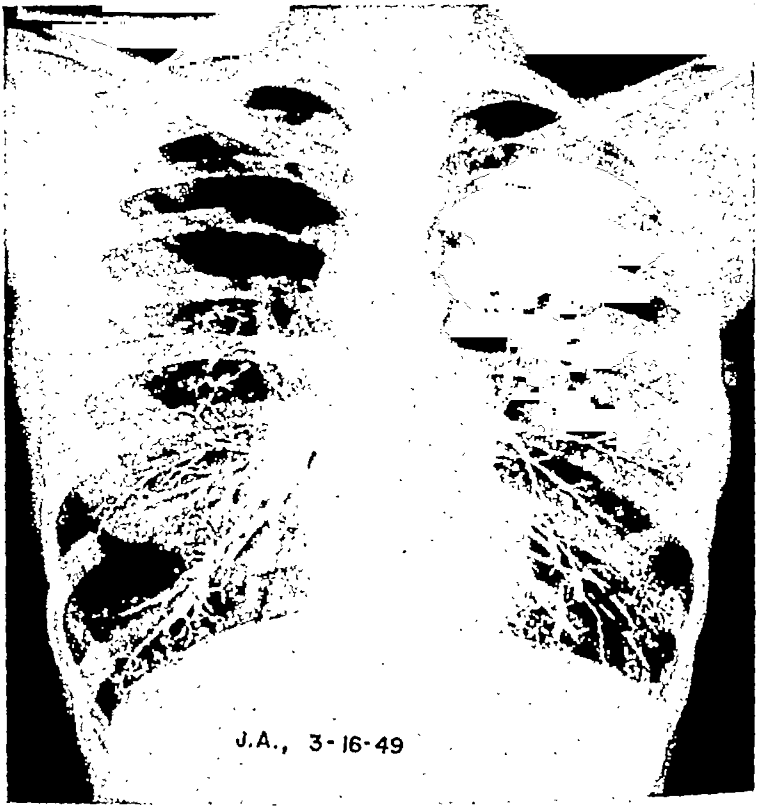
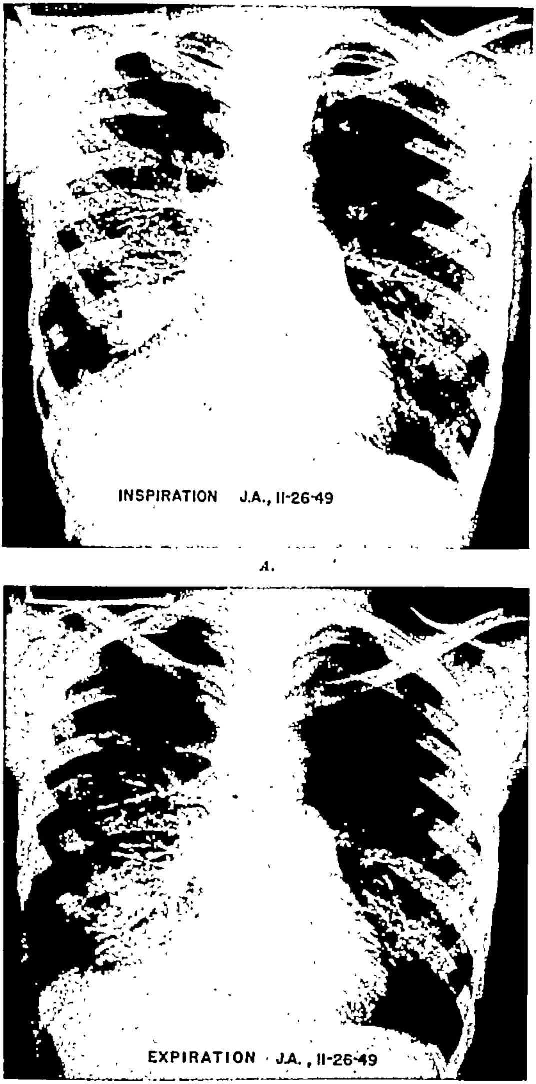


Fig. 9 (Case 3, J. A.).—Preoperative bronchogram revealing the moderate bronchospasm of asthma.

She was followed in the allergy clinic until August, 1949, on the average of two visits per month, where she had received all known specific and nonspecific therapeutic measures without relief. On her first two hospitalizations, February and March 1945, she was admitted to the ear, nose, and throat service. Multiple antrotomies were performed, and the anterior half of both middle turbinates, the polyps, and all polypoid tissue were removed. Thereafter she was followed in the ear, nose, and throat clinic, where polyps were frequently removed. On her third, fourth, and fifth hospitalizations, she was admitted to the medical service during the months of March, April, and May, 1949, for periods of seven, eight, and twenty days, respectively, in status asthmaticus. She was having four to five attacks per day, was extremely



A.

B.

Fig. 10 (Case 3, J. A.).—Bronchograms obtained during inspiration (*A*) and expiration (*B*) following bilateral parasympathectomy of the bronchial tree. Note the persistence of generalized bronchospasm during both phases of respiration.

dyspneic, incapacitated, and "adrenalin fast." There had been no weight gain in four years. The nasal mucosa was edematous and associated with mucopurulent discharge. She was round-shouldered, and there was a moderate dorsal kyphosis. The clavicles were prominent and the accessory respiratory muscles were active. The anteroposterior diameter was increased. The chest was hyperresonant and wheezes were heard throughout both lung fields. Expiration was prolonged.

Pertinent laboratory findings revealed an eosinophilia ranging from 2 to 8 per cent. Roentgenograms showed a pansinusitis and a bronchogram revealed generalized bronchospasm (Fig. 9). She was placed in an oxygen tent, received aminophyllin, grains 7½ every 3 hours, and aerosol and systemic antibiotics without relief. Status asthmaticus continued, and a surgical consultation was requested in regard to the feasibility of bilateral vagotomy. Frequent stimulation of the trachea with a nasal catheter and subsequent aspiration appeared to be responsible for interrupting the asthmatic cycle. Inasmuch as medical, allergic, and psychotherapeutic measures had been unsuccessful, she was discharged and instructed to return during a period of remission for vagotomy. She was readmitted June 1, 1949. The vital capacity was 1,300 c.c. There was a 5 per cent eosinophilia in the peripheral blood. An electrocardiogram revealed a sinus tachycardia of 130.

On June 3, using a posterolateral incision, the left chest was entered through the fourth interspace. After identification of the recurrent laryngeal nerve at the arch of the aorta, the vagus nerve was transected immediately below this point. Electrocardiographic studies revealed no effects due to vagal irritation or transection. For the first two postoperative weeks her asthma appeared to be improved, although on the third and fourth days she complained of epigastric fullness. A bilateral bronchogram performed on the tenth postoperative day revealed generalized bronchospasm on both sides of the bronchial tree. An x-ray examination of the chest twenty-four hours later revealed approximately the same amount of Lipiodol in the alveoli on the left as on the right, although a small amount of oil was remaining in one of the left lower lobe bronchi. Toward the end of her hospital stay, the attacks occurred with increasing frequency, often precipitated by conversation and diagnostic measures.

While obtaining a gastric motility tracing on her twenty-first postoperative day she had another asthmatic attack. Five minutes after injecting the right vagus trunk in the cervical region with 1 per cent Novocain, the asthmatic attack ceased. The gastric motility tracing which had been normal until this time demonstrated complete absence of peristalsis. A postoperative electrocardiogram revealed a sinus tachycardia of 110. Daily vital capacities averaged 1,100 c.c., 1,900 c.c., 1,200 c.c., and 1,400 c.c. during the first, second, third, and fourth postoperative weeks, respectively. She was discharged to return for further evaluation. No improvement was noted, and on the basis of the previous vagus injection, it was decided to cut the pulmonary branches of the right vagus nerve. She was readmitted on Oct. 31, 1949, and the operative procedure was performed as outlined in Case 2. Postoperatively she continued to have one to two attacks per day, although not as severe. Coughing paroxysms were definitely decreased. On the sixteenth postoperative day a bilateral bronchogram was performed which demonstrated a generalized bronchospasm during both the inspiratory and expiratory phases of respiration (Fig. 10, *A* and *B*). That night she had another attack of asthma, became comatose, and despite the most vigorous attempts at resuscitation, tracheal aspiration and stimulants, she died. Permission for post-mortem exmination was not granted.

DISCUSSION

A study based on three patients is insufficient from which to draw definite conclusions as to the efficacy of bilateral parasympathectomy in the surgical treatment of bronchial asthma. In addition an adequate period has not elapsed postoperatively to allow for more than a preliminary report. One patient (E.C.) states she is "cured," another (J.A.) is dead, and the remaining patient (D.T.) is slightly but definitely improved. In general, the results are only a little better than equivocal. However, one must remember that only those asthmatic patients failing to respond to all other known measures were subjected to this operative procedure, and thus the study represents an attempt at salvage of these patients.

The most impressive finding in this investigation was the persistence of bronchospasm after bilateral interruption of the so-called "bronchomotor nerves." Regardless of the clinical result bronchospasm was demonstrable in all three patients after the instillation of Lipiodol. Bilateral parasympathectomy of the bronchial tree, thus, resulted in no change in the caliber of the bronchi. This evidence is confirmatory of our previous studies in which unilateral vagotomy performed immediately below the origin of the recurrent laryngeal nerve was without effect on the caliber of the homolateral bronchial tree. This suggests that our present concept of the neurogenic origin of bronchial asthma is not valid.

All three patients noted that cough had decreased greatly following surgery. This observation is in accordance with our previous studies in which it was demonstrated that the cough reflex arising from stimulation of the homolateral bronchial tree had been abolished following unilateral vagotomy performed above the origin of the pulmonary plexus. Since the cough reflex, the ciliary activity of the bronchial mucosa and the respiratory movements of the bronchial tree are considered to be the more important physiologic mechanisms in the maintenance of a patent bronchial tree, it must be assumed that abolition of the bronchial nerve impulses resulting in initiation of the cough reflex does not impair the efficiency of clearance of tracheobronchial secretions. Previous investigation, reviewed briefly later, revealed that unilateral vagotomy did not *impair the clearance of secretions from the homolateral bronchial tree.* This was demonstrated by a bronchographic study. Fortunately the patients with unilateral vagotomy serve as their own controls in that clearance of secretion from the denervated homolateral bronchial tree can be compared with the clearance of secretions from the normal contralateral bronchial tree. Caution was exercised in the performance of the bronchograms so that an equal amount of Lipiodol was introduced into each side of the bronchial tree by using a tracheal catheter. One to seven days after bronchography, posteroanterior chest roentgenograms were obtained in order to determine the residual amount of radiopaque material remaining in both sides of the bronchial tree. If the residual oil in each side was found to be of the same amount then it could be assumed that unilateral vagus section had not impaired the efficiency of clearance of secretion from the homolateral bronchial tree. With one exception there was no pooling of secretion, such as would be evidenced by a greater residuum of oil on the homolateral side. Therefore, in the absence of the cough reflex, it appears that the ciliary activity of the bronchial mucosa in conjunction with the respiratory movements of the bronchi is capable of effecting a satisfactory clearance of tracheobronchial secretions. That such is the case in the present investigation is demonstrated in the first two patients, D.T. and E.C., in whom postbronchography chest roentgenograms revealed no impairment of tracheobronchial clearance following bilateral parasympathectomy of the bronchial tree. Unfortunately we were unable to obtain these studies in Case 3 (J.A.). Such studies in conjunction with a post-mortem examination would have been of the greatest importance in that investigators have reported death in asthmatics to be due to ciliary insufficiency. Hilding[24] found a metamorphosis of the normal columnar ciliated cells to goblet cells with a resultant loss of ciliary mechanism in thirty-nine fatal cases of asthma. It is logical to assume that the death of J. A. was probably due to the surgical abolition of the cough reflex in the presence of ciliary insufficiency. Because of this fact bilateral parasympathectomy of the bronchial tree should be avoided in patients having unusually severe asthma of long duration in whom metamorphosis of the normal ciliated epithelium has probably occurred. In the future, the selection of asthmatic patients to be subjected to this procedure should be made cautiously.

For a number of years investigators have demonstrated the occurrence of pulmonary edema immediately following bilateral vagotomy in experimental animals. The pathogenesis of this phenomenon has been the subject of considerable debate, and has suggested the possibility that a true "neuropathic" pulmonary edema may exist in man. That such studies do not apply to man is indicated by the absence of pulmonary edema in the preceding three cases following bilateral parasympathectomy of the bronchial tree. In addition, it is of interest that this procedure did not cause any discernible cardiovascular effects, transient or permanent, as evidenced by a comparison of electrocardiographic tracings obtained before, during, and after surgery.

In an attempt to explain the good clinical results obtained in Case 2 (E.C.) we have postulated that the occurrence of her asthmatic attacks is dependent upon the presence of two factors: a local factor (infection, hypersensitiveness, or irritation) within the bronchial tree, and a central factor. Theoretically, the local factor by itself is not capable of initiating the asthmatic paroxysm; however, in the presence of the local factor, the asthmatic attack may be precipitated by an increased number of bronchomotor impulses carried in the vagus nerve, caused by an emotional disturbance. Bilateral interruption of the nervous pathways transmitting the central factor would then inhibit the occurrence of the asthmatic attacks. Support of this theory is derived from the fact that she was free of asthma until a bilateral bronchogram was performed. Theoretically, the instillation of Lipiodol, acting as a foreign body, precipitated an attack by increasing the bronchomotor impulses through stimulation of the postganglionic vagal fibers distal to the site of previous transection.

According to the hypothesis presented earlier in this report, the ideal procedure in the surgical treatment of intractable bronchial asthma is a bilateral transection of the vagus nerves immediately below the origin of the recurrent laryngeal nerves. However, the severity of the gastrointestinal symptoms resulting from such a procedure, as in Case 1 (D.T.), does not justify its continued application. Accordingly, the surgical procedure was modified to the transection of one vagus trunk below the recurrent laryngeal nerve and the cutting of the pulmonary branches of the contralateral vagus nerve, as performed in Cases 2 and 3 in two stages. No discernible gastrointestinal or cardiovascular effects were noted. At present we believe this procedure to be relatively innocuous and without any serious immediate morbidity. As pointed out previously, the application of this procedure should be made cautiously in that the selection of patients should exclude those probably having ciliary insufficiency. The possibility of performing this procedure through a unilateral approach is being considered. Although no conclusions as to the value of bilateral parasympathectomy of the bronchial tree can be made from such a small series of patients, we believe that the good clinical results obtained in Case 2 (E.C.) justify a continuation of the surgical attempts in the treatment of intractable bronchial asthma.

SUMMARY

1. A review of the literature pertinent to the anatomy and physiology of the extrinsic pulmonary nerves as related to bronchial physiology is presented.

2. The present concept of the pathologic physiology of bronchial asthma as related to its neurogenic origin is discussed.

3. The surgical procedures previously performed by various investigations on the extrinsic pulmonary nerves in cases of intractable bronchial asthma are briefly reviewed.

4. Three patients with intractable bronchial asthma were subjected to bilateral parasympathectomy of the bronchial tree. Although the clinical results are little better than equivocal, bronchospasm was still present in all three patients as demonstrated by bronchography.

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(See discussion on page 591.)

THERAPEUTIC STATUS OF PULMONARY AUTONOMIC NERVE SURGERY

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THE possible application of surgery of the autonomic nervous system to bronchial asthma has long been considered and sporadically applied. Such procedures as stellate ganglionectomy[1] and high dorsal sympathetic nerve block[2] have been suggested for application in this disease since 1923. Rienhoff and Gay[3, 4] reported promising results following procedures attempted toward complete denervation of the lung by excision of the posterior pulmonary plexus in 1938. In 1947, Carr and Chandler[5] presented the long term results following dorsal sympathectomy for bronchial asthma. In the discussion of this paper, the possible value of autonomic surgery in other pulmonary conditions such as emphysema[6] was considered. Blades,[7] in 1948, presented a review of the history of the surgical approaches utilized in bronchial asthma and presented the early results of a considerably more radical method of pulmonary denervation in the surgical management of this disease. Bailey[8] has also stressed the importance of more radical measures. A distinct contribution to our knowledge of the physiologic effect of the vagus upon the bronchial tree has recently been presented by Curtis and Klassen.[9] They have demonstrated the transmission of sensations of bronchial discomfort along vagal pathways and have applied this knowledge in the utilization of high vagus transection as a palliative measure for the intractable cough of nonresectable bronchiogenic carcinoma.

We are not as yet in full possession of a knowledge of the role which the autonomic nervous system plays in regard to bronchial physiology. It is admittedly difficult or impossible to apply experimental studies upon the autonomic nervous system of animals to a satisfactory understanding of the physiology of this nervous system in the human being. The reported results of surgery of the autonomic nervous system in the treatment of bronchial asthma in the human being have so far been unable to show any true uniformity.

The surgery of the dorsal sympathetic chain has been quite comparably done by different authors. However, when one studies the reports relative to attempts at complete pulmonary denervation, it becomes obvious that there is a considerable discrepancy in the completeness with which this procedure has been carried out. Certainly prior to 1947 there had not been satisfactory recognition of the number and importance of fibers going from the vagus nerve to the pulmonary hilus from a level at and above the recurrent laryngeal nerve. The experiences of ourselves and others make us feel that considerable stress

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should be laid upon the fibers which may descend to the hilus from the recurrent laryngeal nerve itself and also those which arise from the main vagal trunk above the recurrent laryngeal nerve. In the main, these fibers tend to go to the anterior portion of the hilus and particularly are distributed in the tissues about the pulmonary artery and superior pulmonary vein. Blades has emphasized the number of sympathetic nerve fibers which may come across from the contralateral side of the chest via the pulmonary artery. He also emphasized the frequency with which both vagal and sympathetic fibers may enter the lung route through the pulmonary ligament. It is vitally important, therefore, in any consideration of the application of autonomic surgery to pulmonary disease that the specific degree of completeness of pulmonary denervation be emphasized. In 1945, we felt that we were carrying out a more complete denervation of the lung when we were severing the higher fibers from the vagus and cleaning the hilus down to the level of the pulmonary ligament. However, we now know that this is an incomplete pulmonary plexectomy or denervation and prior to 1949 we can only find one of our patients in whom we can consider that a truly complete plexectomy had been carried out. That was in 1945, when we first added perivascular sympathectomy and complete transection of the pulmonary ligament. In retrospect we find that we had much more benefit in this individual patient.

We feel, therefore, that it is important to classify the denervation procedures in four separate categories. First, there is dorsal postganglionic sympathectomy involving the removal of the second through the fifth and occasionally through the seventh sympathetic ganglia. Second, there is transection of the vagus nerve just below the level of the recurrent laryngeal nerve which must admittedly leave even some distinct fibers of the vagus going into the pulmonary hilus; this we call "high vagus transection." Third, there is the operation of completely transecting all visible fibers of the vagus going into the hilus of the lung except for those going through the pulmonary ligament and without stripping of the sympathetic fibers coming through the perivascular sheaths; this procedure we will classify as "partial or incomplete pulmonary plexectomy." Finally, there is the most complete type of pulmonary denervation, that described by Dr. Blades, which we classify as "complete pulmonary plexectomy or denervation."

The attacks upon the sympathetic, parasympathetic, and combined autonomic nervous systems have made us feel that a comparative study of the results of the application of these different methods in one clinic might prove valuable in a further understanding of this subject. In the discussion of Dr. Carr's paper before this Society in 1947, both Dr. Ralph Adams and one of us (O. A. A.) drew attention to instances of apparent benefit of autonomic surgery in relation to pulmonary emphysema. We have tried to apply autonomic surgery in other types of pulmonary disease and wish to consider the role of such an approach in these other diseases at this time. To date we have carried out autonomic nerve surgery as a solitary procedure or in conjunction with other surgical procedures in relation to pulmonary disease in 72 patients.

We are fully cognizant of the difficulty in evaluating the results of autonomic surgery in relation to pulmonary disease. In patients with severe dyspnea or with asthma there is almost constant associated personality disturbance. It is frequently difficult or impossible to determine whether this personality disturbance anteceded the pulmonary difficulty or presented as a consequence of prolonged pulmonary disability. We have attempted in all cases to evaluate the personality status and in almost all patients have carried out a prolonged trial of conservative measures directed toward (1) reassurance with psychotherapy, (2) improvement in associated pulmonary suppuration by endoscopy under ether anesthesia, chemotherapy, chest exercises, and expectorants, and (3) improvement in the breathing habits, particularly by expiratory chest exercises. In many instances there has been a striking result from this conservative type of approach. No patient was subjected to autonomic surgery until we were satisfied that this type of approach had failed. One must also emphasize that in the application of a procedure which is not necessarily an accepted one the caliber of patients treated consisted in the main of those with very far advanced and intractable disease.

As our experiences have grown with the application of these procedures we have become increasingly impressed with the need for objective studies in regard to pulmonary function both before and after surgical interference. Adequate pulmonary functional studies have only recently been available to us, and we feel that further experience with this method of study and of longer follow-up of these objectively studied patients should be carried out before presenting specific results from this more objective approach. For the past five years we have tried to apply an admittedly very limited method of study in regard to these patients; namely, to study the effect of various drugs upon the individual's vital capacity before treating the patient either by the conservative or combined conservative and surgical approach. The only value noted in this study is that we have been impressed by the considerable increase in vital capacity in patients with bronchial asthma following injection of epinephrine, Isuprel, or aminophylline, and it also appears to be an essentially uniform finding in the study of patients with extensive bilateral emphysema. More detailed studies are being carried out by the pulmonary function laboratory to investigate further the role of associated bronchospasm in pulmonary emphysema. At present, we must state that we cannot accept the premise that bronchospasm is not an important and probably integral part of diffuse interstitial or bullous emphysema or a combination of those types of emphysema.

CLINICAL OBSERVATIONS

1. Bronchial Asthma.—Having been stimulated by Dr. Carr's observations in 1947, we began a series of patients with different types of autonomic surgery in an attempt to control intractable bronchial asthma. The procedures utilized consisted of (1) upper dorsal postganglionic sympathectomy, (2) high vagotomy, (3) plexectomy which we then thought was complete and now must consider as partial or incomplete plexectomy, and (4) a more recent group applying the complete plexectomy procedure. It must be stressed that certain postoperative mortalities which occurred early in this study appear to have been avoidable in view of subsequent experience. Patients with intractable bronchial asthma present a difficult physiopathologic entity to treat, and it would appear important to discuss these early deaths and the experiences obtained therefrom.

In one patient there was produced a contralateral tension pneumothorax during the operative procedure which in retrospect can probably be attributed to considerable difficulty in anesthesia induction. Any anesthetic agent prone to produce bronchospasm must be avoided in asthmatic patients. The particular drugs to avoid are sodium pentothal and cyclopropane. The use of a good basal anesthetic such as rectal ether or avertin has met with considerable improvement in regard to anesthesia induction in our experience. This patient with a tension pneumothorax on the contralateral side died twelve hours postoperatively during the insertion of a thoracentesis needle. The actual cause of death was attributed to air embolism. In two other patients there was an acute obstructive type of emphysema, and since we were reluctant at that time to bronchoscope this group of patients, they did not undergo what we feel from autopsy findings would have been a life-saving bronchoscopy. We feel that it must be stressed that the bronchoscope is an almost routine measure in the postoperative course of these patients. In a further instance a patient who had undergone an initial procedure on the left side with a fairly good immediate result died following the operation upon the second side carried out after a four-month interval, due to improper handling of a postoperative cardiac arrhythmia. This patient developed a rather severe auricular fibrillation and was given 0.8 mg. of Cedilanid intravenously and this rhythm converted to a ventricular tachycardia. A second dose of 0.8 mg. of Cedilanid intravenously was given in the presence of this type of rhythm with immediate transformation of the ventricular tachycardia into a fatal ventricular fibrillation. It must be stressed that pre- and postoperative electrocardiograms are of considerable value in the handling of postoperative complications in this patient group. Two other deaths occurred in this series; both of these patients were over 70 years of age with completely intractable asthma. Each patient had shown a poor response following sympathectomy on one side and died following the operation upon the contralateral side. Both these patients had marked pulmonary destruction and suppuration and also advanced coronary heart disease. In retrospect, one must consider that despite the apparent hopeless situation that these patients were too severe risks for the operative procedure.

A. Results in the Surgical Treatment of Bronchial Asthma With Sympathectomy Alone: The results obtained in the application of upper dorsal postganglionic sympathectomy in a group of fourteen patients with intractable bronchial asthma are presented in Table I. In this group of patients, 5 were subjected to bilateral sympathectomy, 2 of whom died and consist of the 2 aged patients previously mentioned. These 2 patients and one other who has been followed for approximately twenty-two months must be considered as

TABLE I. BRONCHIAL ASTHMA—SYMPATHECTOMY ALONE

NUMBER OF PATIENTS		RESULTS				
		FAILURE	FAIR	GOOD	CURED	DEATHS
Left Side	7	2	3	0	2	0
Right Side	2	0	0	0	2	0
Bilateral	5	3	2	0	0	2
Total	14	5	5	0	4	2*

*Deaths are included in failures.

complete failures. The 2 patients who died were observed for three- and four-month intervals between operations, and no satisfactory response had been obtained from the initial procedure. Two patients had upper dorsal postganglionic sympathectomy on the right side only and both of these patients have shown a very satisfactory follow-up completely free of asthma eighteen and twenty-six months, respectively. Seven patients were subjected to a left upper dorsal sympathectomy alone. This group has produced two complete failures with persistent asthma of equal severity to that before operation. Three have had fair results in which the degree of asthma has been decreased at least 50 per cent, and 2 have continued to be completely free from asthma for twelve and fifteen months, respectively.

This group of patients was then re-evaluated as shown in Table II to try to find a common denominator in regard to those patients who had a failure, a fair or good result, and those who had become asthma-free. In every instance it was found that those who had become cured or free of their asthma did not have major associated pulmonary suppuration or destruction. In those having such major suppuration there were four complete failures and four in whom the result could be classified as only fair. In this group repeated chemotherapy has been utilized to help control the postoperative situation and must receive a considerable proportion of the credit for the "fair" group of results. Three patients undergoing this procedure, who presented a complete failure postoperatively, were serious narcotic addicts in whom the addiction could not be controlled either before or after operation. The 4 patients who obtained apparent complete cure were derived from a group who had associated disease in the thorax and who required an intrathoracic procedure essentially for this associated disease and the sympathectomy was carried out in conjunction because of known associated moderately severe or severe bronchial asthma. The 4 patients who could be classified as cured had sympathectomy of unilateral type

TABLE II. BRONCHIAL ASTHMA—SYMPATHECTOMY ALONE (ROLE OF ASSOCIATED DISEASE)

	NO. OF PATIENTS	RESULTS		
		FAILURE	FAIR	CURED
Diffuse Suppuration	8	4	4	0
Narcotic Addiction*	3	3	0	0
Miscellaneous Disease†	6	1	1	4
Total	14	8	5	4

*Two narcotic addicts had diffuse suppuration.

†Carcinoma of esophagus; emphysema; cardiospasm; neurofibroma; carcinoma lung, peripheral; carcinoma, lung, with suppuration.

in conjunction with (1) an operation for cardiospasm, (2) another with a posterior mediastinal tumor, namely a neurofibroma, (3) another had a peripheral type of inoperable pulmonary carcinoma, (4) while the other had an esophageal resection for primary carcinoma of that organ. The patient with inoperable pulmonary carcinoma lived for five months without any recurrence of what previously had been constant bronchial asthma. The patient having cardiospasm had had intractable asthma for two years prior to operation and has remained completely free of asthma for eighteen months. The patient in whom a neurofibroma was removed had not been free of asthma for forty-three years prior to operation and has remained free of asthma now for nineteen months. The patient having a resection of the esophagus for carcinoma has been observed fourteen months postoperatively, and he is completely relieved of bronchial asthma which had been constantly present for twenty-two years previously. One patient in whom the result can be classified as a failure had a bronchiogenic carcinoma with considerable suppuration and continued to have constant asthma for seven months following the procedure. One patient having a fair result had most extensive pulmonary emphysema and also diffuse suppurative disease. It is our impression, therefore, from this patient group that a good result cannot be obtained from sympathectomy alone in patients having diffuse destructive pulmonary suppuration. An equally hopeless group is the patient having bronchial asthma who has become a severe narcotic addict. The happiest results from sympathectomy appear to be those in whom no suppurative disease has occurred.

B. Surgical Treatment of Bronchial Asthma by the Use of Varying Degrees of Pulmonary Plexectomy: Results obtained by the use of attempts at pulmonary denervation or by transection of the vagus nerve just below the level of the recurrent laryngeal nerve are presented in Table III. There were 18 patients in this group. Two patients had high transection of the vagus, and the results in both these patients were essentially unsatisfactory and at best can be classified as fair. With the application of partial or incomplete plexectomy or denervation there were 12 patients subjected to this procedure. Four of these patients died within the first three weeks following operation and a fifth died without relief of asthma ten weeks following surgery. This last-mentioned patient had severe associated diffuse pulmonary suppuration and obtained no benefit whatsoever from the procedure. One patient having a partial plexectomy was distinctly improved and has been followed over one year after

TABLE III. BRONCHIAL ASTHMA—PLEXECTOMY OR VAGOTOMY

PROCEDURE	NO. OF PATIENTS	RESULTS				
		DEATHS	FAILURE	FAIR	GOOD	CURED
High Right Vagotomy	2			2		
Left	1	1				
Partial Plexectomy						
Left	9	2	4	1	2	
Bilateral	3	1	1		1	
Complete Plexectomy						
Left	3			1	1	1
Total	18	4	5	4	4	1

surgery; the severity and frequency of asthmatic attacks have been considerably attenuated. The 3 patients in this group classified as good results could be classified in the cured group except for rare extremely mild asthmatic attacks not requiring drugs in two instances and only rarely requiring drugs in the other. The 3 patients undergoing complete pulmonary denervation according to the methods of Blades have shown much better results. One is apparently cured, 1 is very markedly improved with rare asthma attacks, and the one patient having only a fair result has associated diffuse pulmonary suppurative destruction.

C. Surgical Treatment of Bronchial Asthma by Means of Autonomic Nerve Surgery Plus Resection of "Trigger Areas." (See Table IV): It has been the experience of the authors to encounter 13 patients in the past three years who had severe bronchial asthma in association with demonstrable localized areas of pulmonary destruction. It is felt from clinical experience with this group that these localized areas in some way played a productive role in relation to the patient's bronchial asthma and have therefore been classified as "trigger areas." Prior to this group we had experience with lobectomy for bronchiectasis in 5 patients having associated bronchial asthma in whom the bronchial asthma persisted following the operative procedure. In this group of 13 patients, 8 underwent some form of sympathectomy in association with segmental pulmonary resection or total lobectomy. There were none in this group which could be classified as a complete failure in regard to the effect of the operative procedure upon the patient's associated bronchial asthma. Three had a result which could be classified as only fair; 2 of these had bilateral bronchiectasis with bilateral segmental resection but the sympathectomy was confined to one side. The third in this group of fair results is a severe frank psychotic. Two patients having good results with resection of "trigger areas" plus a left dorsal postganglionic sympathectomy have had very rare attacks of asthma following operation not requiring drugs. One patient with bilateral bronchiectasis undergoing bilateral surgery had concomitant bilateral sympathectomy with an apparent cure. In all those patients achieving an apparent cure in this group there has been complete removal of demonstrable areas of pulmonary destruction. One patient had a right upper lobectomy for bronchiectasis and an associated high right vagus nerve transection because of antecedent severe bronchial

TABLE IV. BRONCHIAL ASTHMA—AUTONOMIC SURGERY PLUS RESECTION OF TRIGGER AREAS*

	NO. OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	CURED
Sympathectomy					
–Right	2		1		1
–Left	5		2	2	1
–Bilateral	1		0		1
High Right Vagus Resection	1			1	
Complete –Right	1				1
Plexectomy –Left	3				3
Total	13	0	3†	3	7

*Eleven of these patients had associated segmental resection or total lobectomy for bronchiectasis. Three had excision of major localized tension bullae.

†Two of this group have suppurative disease still present on the contralateral side. One patient is frankly psychotic.

asthma, and she has been followed for twenty-six months and has had only two extremely mild attacks of asthma during that interval. Four patients have been subjected to resection of apparent "trigger areas" along with complete pulmonary denervation and in all 4 of these patients an extremely satisfactory result has been obtained. Of the 13 patients in this group, 11 had their "trigger areas" consisting of pulmonary segments or lobes destroyed by bronchiectasis. The two remaining patients had local areas of major emphysematous bullae.

In summary (see Table V) we present experience with 45 patients with severe bronchial asthma in whom autonomic surgery or a combination of autonomic surgery plus removal of "trigger areas" of pulmonary destruction have been carried out. The most beneficial results have been obtained in the patient group in whom resection of areas of pulmonary destruction plus a complete pulmonary denervation has been performed. Markedly beneficial results have been obtained in those patients having removal of "trigger areas" of pulmonary destruction plus either parasympathetic or sympathetic interruption. If the operative procedure is to be confined purely to the interruption of the autonomic nervous system, the patient should neither have evidence of serious diffuse suppurative pulmonary destruction, nor have evidence of major associated psychic disturbance such as narcotic addiction.

TABLE V. BRONCHIAL ASTHMA—COMPARATIVE RESULTS FOLLOWING DIFFERENT SURGICAL PROCEDURES

PROCEDURE	NO. OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	CURED
Dorsal Sympathectomy	14	5	5	0	4
Partial Plexectomy	15	9	1	3	0
Complete Plexectomy	3	0	1	1	1
Sympathectomy plus Excision Area Lung Destruction	8	0	3	2	3
Partial Plexectomy plus Excision Area Lung Destruction	1	0	0	1	0
Complete Plexectomy plus Excision Area Lung Destruction	4	0	0	0	4
Totals	45	14	10	7	12

2. Pulmonary Emphysema.—

The authors are in the process of carrying out objective studies in a group of patients with severe pulmonary emphysema either of the primarily bullous type or of the interstitial type of emphysema. It is felt too early to be able to present objective results in this group of patients, but the preliminary clinical results of this group are presented in Table VI. Several of these patients can be classified to have what is termed "vanishing lung disease" and a satisfactory evaluation of this group will have to be done both in regard to symptomatology, objective studies, and the future progress of the underlying "vanishing lung disease." We are able to state at the present time that symptomatic cure has been obtained in four patients having autonomic surgery in association with resection of major bullae and in these patients at operation there was found

TABLE VI. PULMONARY EMPHYSEMA

PROCEDURE	NO. OF PATIENTS	DEATH	FAILURE	FAIR	GOOD	SYMPTOMATIC CURE
Sympathectomy						
-Left				2	1	
-Right						
-Bilateral			1		2	
Plexectomy						
-Left Partial						
-Left Complete						
-Right Complete						
Bullae						
-Sympathectomy						2
-Partial Plex.					1	2
-Complete Plex.				1		
Total	12	0	1	3	4	4

to be associated diffuse interstitial emphysema. Four patients have apparently good results from left sympathectomy in one, bilateral upper dorsal sympathectomy in two, and partial pulmonary denervation plus removal of emphysematous bullae in one. Three patients have shown only fair results to date, and one must be characterized as a frank failure. It is felt that further objective investigation and further follow-up will be required in this group before being able to present any conclusions. It is important to stress that we do feel that we see a considerable amount of bronchospasm in association with extensive emphysema and that occasional patients apparently benefit from autonomic nerve surgery in this disease. It is also felt that some patients with major emphysematous bullae will benefit by using some denervation procedure in conjunction with resection of the bullae if there is preoperative evidence of major bronchospasm.

3. Autonomic Surgery as a Palliative Measure in Inoperable Bronchiogenic Carcinoma.—

The results of the application of different types of autonomic surgery in patients who, on exploratory thoracotomy, were found to have inoperable carcinoma of the lung are presented in Table VII. There are 10 patients in this group. In 1946 and 1947, we carried out upper dorsal sympathectomy at the conclusion of the exploratory operation in 6 patients and during the follow-up period achieved no benefit in regard to severe cough in 5 of these patients. In 1 patient there appeared to be a considerable benefit in regard to cough, but this patient also had associated bronchial asthma, and this symptom was apparently relieved by the operative procedure. Since 1948, we have utilized high vagus resection in 4 patients with bronchiogenic carcinoma and

TABLE VII. INOPERABLE BRONCHIOGENIC CARCINOMA—EXPLORATION PLUS AUTONOMIC SURGERY

PROCEDURE	NO. OF PATIENTS	EFFECTIVE PALLIATION	NO PALLIATION
Sympathectomy	6	1*	5
High Vagus Resection	4	4	0
Total	10	5	5

*This patient had asthma and was relieved for five months.

have appeared to obtain effective palliation in regard to cough in each patient of this group. It is our impression, therefore, from a study of these 10 cases that upper dorsal sympathectomy does not have any usefulness as a palliative measure in regard to cough, while high vagus resection can be of considerable value. It should be noted that we have seen 3 patients with bronchiogenic carcinoma in whom at autopsy the vagus nerve on the involved side had undergone complete destruction, and these patients' terminal courses were rather strikingly free of intractable cough.

4. Role of Associated Autonomic Surgery Along With Pulmonary Resection in Certain Cases of Bronchiectasis.—

To date the authors have tried the application of autonomic nerve surgery in association with pulmonary resection in a group of 14 patients with bronchiectasis. The patients with bronchiectasis in whom this operative procedure was considered were only those patients with bronchiectasis showing a major degree of associated allergy and bronchospasm. Many of these patients had actual asthmatoid attacks, but those we did not classify as true asthma. There was marked evidence on clinical examination of diffuse bronchospasm which was also shown on bronchogram. It had been our experience to have several patients of this type in whom lobectomy had been carried out and who had palliation of the major bronchiectatic symptoms but continued to have some wheeze, some bronchorrhea, and other complaints apparently referrable to allergy and bronchospasm. In this group of patients (see Table VIII) upper dorsal sympathectomy was carried out in association with lobectomy in eleven. A satisfactory beneficial result was obtained in 9 while the 2 patients classified either as a failure or as fair had bilateral disease and bilateral resection but only unilateral sympathectomy. The patients having most satisfactory results were 4 who had unilateral bronchiectasis with associated unilateral sympathectomy and 3 who had bilateral resection associated with bilateral autonomic surgery. It is our impression from this group that this type of patient does benefit by autonomic nerve surgery either of sympathectomy or pulmonary plexectomy type, and if the patient has bilateral disease then bilateral autonomic nerve interruption should be carried out.

TABLE VIII. BRONCHIECTASIS—PLUS DIFFUSE BRONCHOSPASM AND ALLERGY (PULMONARY RESECTION PLUS AUTONOMIC SURGERY)

PROCEDURE	NO. OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	CURED
Sympathectomy	11	1*	1*	4	5
Partial Plexectomy	3			1	2
Total	14	1	1	5	7†

*These patients had bilateral segmental resection but autonomic surgery only on one side.
†Three of the seven patients cured had bilateral resection and bilateral autonomic surgery.

5. Sympathectomy in the Treatment of Severe Bronchorrhea.—

Results in 2 patients having severe bronchorrhea in whom upper dorsal sympathectomy was carried out are presented in Table IX. These patients both had very copious production of sputum with considerable associated wheezing. Results in these 2 patients following sympathectomy appear to be quite striking in the reduction of the 24-hour sputum production. These 2 patients are presented purely *as a matter of interest only, and further study of this* patient group will be required before making any conclusions.

TABLE IX. SYMPATHECTOMY FOR BRONCHORRHEA

TYPE	NUMBER OF PATIENTS	PRODUCTION BEFORE SURGERY	PRODUCTION AFTER SURGERY	DURATION FOLLOW-UP
Unilateral Left D1-7 R 2-5	1	14 oz./24 hr.	3 oz./24 hr.	18 mo.
Bilateral L 2-6	1	24 oz./24 hr.	1½ oz./24 hr.	7 mo.

6. Autonomic Surgery in Conjunction With Decortication and Reconstructive Procedures in the Treatment of Chronic Recurrent Pneumothorax.—

Table X presents the results in 5 patients who were treated by the removal of bullae, overlying peel, and associated autonomic nerve surgery for chronic recurrent spontaneous pneumothorax. The roentgenograms on all 5 of these patients showed considerable associated bilateral emphysema of the interstitial type. These patients, *in all instances, had small bullae on the side of operation* which were felt to be the responsible agent for the recurrent pneumothorax. The addition of autonomic nerve surgery was carried out because of the appearance of the lungs on the x-ray studies as well as the diffuse emphysematous appearance of the lung on the operative side. In all instances these patients showed some demonstrable objective evidence of bronchospasm prior to the operative procedure, and this was also considered as part of the rationale for the addition of the autonomic nerve surgery to the other procedures. This group of patients is again too small to draw any conclusions, but the results appear to be good, and there appears to have been in each instance a considerable decrease in regard to subjective dyspnea which was present between episodes of pneumothorax or prior to the onset of the initial pneumothorax. The major reason for considering this type of procedure is in regard to its possible application for the treatment of pulmonary emphysema.

TABLE X. CHRONIC RECURRENT PNEUMOTHORAX—RECONSTRUCTIVE PROCEDURES PLUS AUTONOMIC SURGERY

PROCEDURE	NUMBER OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	RELIEF FROM PNEUMOTHORAX AND DYSPNEA
Bullae sympathectomy	1				1
Bullae plexectomy	4			2	2
Total	5			2	3

SUMMARY

The authors present their experience with 72 patients in whom some form of autonomic nerve surgery has been applied in relation to pulmonary disease.

Forty-five of these patients were treated for bronchial asthma, and a comparison of the result obtained with sympathectomy, partial or complete plexectomy, and a combination of autonomic surgery plus the removal of "trigger areas" of pulmonary destruction has been presented. Experience with 10 patients utilizing either a sympathectomy or parasympathectomy as a palliative measure in bronchiogenic carcinoma has suggested that parasympathectomy may be of palliative value in this disease. This would appear to confirm the experiences of Curtis and Klassen. A group of patients in whom autonomic surgery has been utilized as a solitary procedure or in conjunction with reconstructive procedures in pulmonary emphysema has been noted. It is the authors' experience that pulmonary emphysema does involve considerable associated bronchospasm. A group of patients with bronchiectasis in whom there was major associated bronchospasm and allergy but who did not have actual asthma is also discussed in regard to the effectiveness of combining autonomic nerve surgery along with pulmonary resection. Five patients having chronic recurrent spontaneous pneumothorax and subjected to reconstructive procedures plus autonomic surgery are described. Finally, 2 patients are noted with severe bronchorrhea, who obtained beneficial results from sympathectomy. Another patient, treated three years ago, had repeated spontaneous pulmonary thromboses on one side, one of which progressed to actual abscess destruction of the right middle lobe. This patient was treated by right middle lobectomy plus dorsal sympathectomy, in view of the presence of arteriolar disease at the time of frozen section. This patient has continued well for three years, but the role of autonomic surgery in this individual patient cannot be evaluated in view of the fact that this patient has also been kept on constant Dicumarol therapy.

CONCLUSIONS

It is our opinion, therefore, from a presentation of the preceding clinical experiences with 72 patients undergoing different types of pulmonary autonomic surgery, that:

1. Distinct beneficial results can be obtained from autonomic nerve surgery in certain types of pulmonary disease, but

2. Considerable objective data by means of pre- and postoperative respiratory function studies will be needed before final conclusions can be made.

However, on the basis of clinical evaluation alone, our experiences suggest that:

3. Autonomic surgery, alone, in the form of complete pulmonary plexectomy or denervation, should be markedly beneficial in the treatment of intractable bronchial asthma unless there is evidence of associated suppurative pulmonary destruction, narcotic addiction, or major psychosis.

4. Autonomic surgery, preferably in the form of complete pulmonary plexectomy, plus excision of "trigger areas" of pulmonary destruction can be markedly beneficial or curative in the treatment of intractable bronchial asthma.

5. The only autonomic surgery of palliative value in the treatment of advanced bronchiogenic carcinoma consists of transection of the parasympathetic fibers (vagus nerve).

6. Bronchospasm plays an important role in the progress of pulmonary emphysema, and autonomic surgery can be of value in the surgical treatment of this disease, particularly as an adjunctive measure to the resection of major bullae.

7. Autonomic surgery in addition to pulmonary resection should be considered in certain bronchiectatic patients with associated marked allergic and bronchospastic tendencies. If such patients require bilateral pulmonary resection, then bilateral associated autonomic surgery is required.

8. Two patients with severe idiopathic bronchorrhea treated by upper dorsal sympathectomy are reported. In both instances marked relief from bronchorrhea was obtained.

9. Autonomic surgery is considered a valuable adjunctive measure in the operative correction of chronic recurrent spontaneous pneumothorax where there is associated interstitial emphysema.

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(See discussion on page 591.)

THE SURGICAL TREATMENT OF INTRACTABLE ASTHMA

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DURING the past thirty-four months 38 patients have been operated upon for severe asthma at the George Washington University Hospital. These cases were selected from approximately 300 patients complaining of the disease. The 38 cases subjected to surgical intervention were completely incapacitated and all known conservative treatment had failed. There were 14 women and 24 men. Their ages varied from 15 to 72 years. The majority of the patients were in the third to the fifth decades of life.

Operations for Asthma.—Kümmell,[1] in 1923, operated upon the sympathetic nervous system for the treatment of severe asthma. His early results appeared to be satisfactory. Approximately one year later, Kappis[2] was equally optimistic about the results of vagotomy for asthma. He divided the vagus on the right side below the level of the recurrent laryngeal nerve. Other surgeons in the past have employed varying techniques for operations on both the sympathetic and parasympathetic systems. Leriche and Fontaine[3] advocated stellate ganglionectomy; and combined operations involving sympathectomy and unilateral vagotomy were employed by Kümmell[1] and others.

Modern revivals of operations on the autonomic nervous systems include Carr and Chandler's[4] reports on the role of dorsal sympathetic ganglionectomy for asthma, Phillips and Scott's[5] use of operations on the parasympathetic system, and later Rienhoff and Gay's[6] contributions concerning bilateral posterior pulmonary plexus resection.

An operation based on the same general approach employed by Phillips and Scott[5] and later by Rienhoff and Gay[6] has been performed in our series.

A left posterolateral incision is made over the fifth rib and after division of the overlying muscles a long segment of the rib is resected. The pleura is incised and the left thoracic cavity opened.

The operation consists of the following steps: 1. Identification of the vagus nerve at the level of the pulmonary plexus. 2. The vagus is freed and retracted gently, but not cut. 3. The pulmonary plexus about the bronchus is destroyed. 4. All branches of the vagus to the pulmonary hilum and lung are divided below the level of the recurrent laryngeal nerve. 5. The esophageal branches and the main trunk of the vagus are saved. 6. The sheaths of the pulmonary artery and veins are removed as much as possible. 7. The pulmonary ligament is divided.

From the Department of Surgery, The George Washington University School of Medicine. Veterans Research Grant from the Research Division, Research and Education Service, Veterans Administration.

Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

The chest wall is reconstructed in layers with an intercostal catheter placed in a separate stab wound and connected to a water-sealed bottle.

There are considerable variations in the patterns of the vagus nerve distribution to the lungs. Observations during 44 operations and dissections on 12 fresh cadavers revealed that the nerve supply to the left lung is considerably greater than the right. On the left side one can usually find two relatively large trunks of the nerve which go in and about the sheath of the pulmonary artery, and two large branches to the left bronchus. In addition, on the left four to eight major filaments are present, distributed between the artery and bronchus. No large branches can be seen going to the sheath of the veins. The nerve supply to the artery is less than that to the bronchus but is abundant.

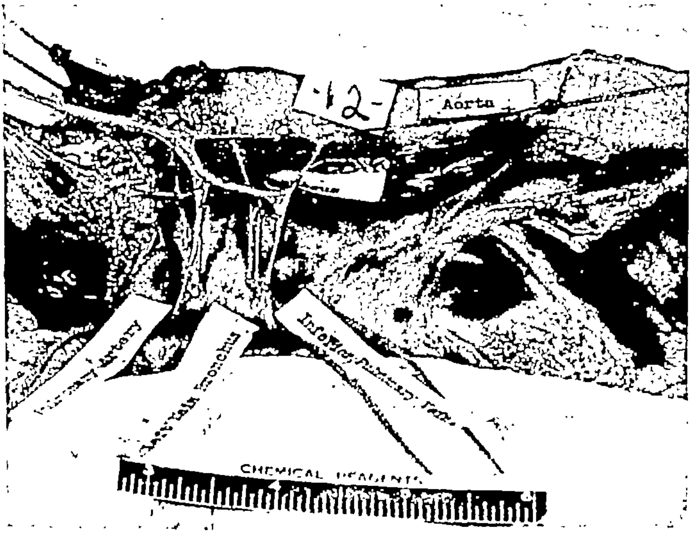

Fig. 1.—Photograph of the distribution of the vagus nerve at the left pulmonary hilum.

On the right side there are usually only two or three main branches and two to four finer filaments. On the right side it appears that the greater portion of the nerve trunks go to the main bronchus, with a meagor supply to the artery as compared to the left side.

Fig. 1 demonstrates a dissection of the left hilum with two major and two minor branches going to artery and bronchus. In Fig. 2, the right hilum is shown with six branches to the bronchus and only one branch of significance to the pulmonary artery.

Selection of Patients.—Only patients who have been completely incapacitated from the disease have been selected for surgical intervention. The diversiform nature of asthma, vague multiple etiological factors and utter lack of precise knowledge of the physiology of the nerve supply of the lungs leaves only an empirical approach for choosing subjects for operation.

The first patient subjected to operation was a 29-year-old white woman, who had had severe asthma for fifteen years. During the four years before the operation she spent the majority of her time in a hospital.

She was first seen in June, 1947, at which time she was receiving oxygen and helium and her condition was critical. Adrenalin, aminophyllin, Benadryl and, finally, ether in oil and avertin were given with no appreciable effect on the status asthmaticus. Finally, 50 c.c. of ether in 1,000 c.c. of saline (100 mg. per kilogram of body weight) was given. The status was broken and about two weeks later the operation was performed. In this first case in which a left-sided denervation was done, there has been complete relief from the disease for thirty-four months. The left side has been the site of initial operation in all subsequent cases because of the relative abundance of nerve supply. Later attempts to treat severe asthma by surgical intervention were stimulated by this original dramatic result.

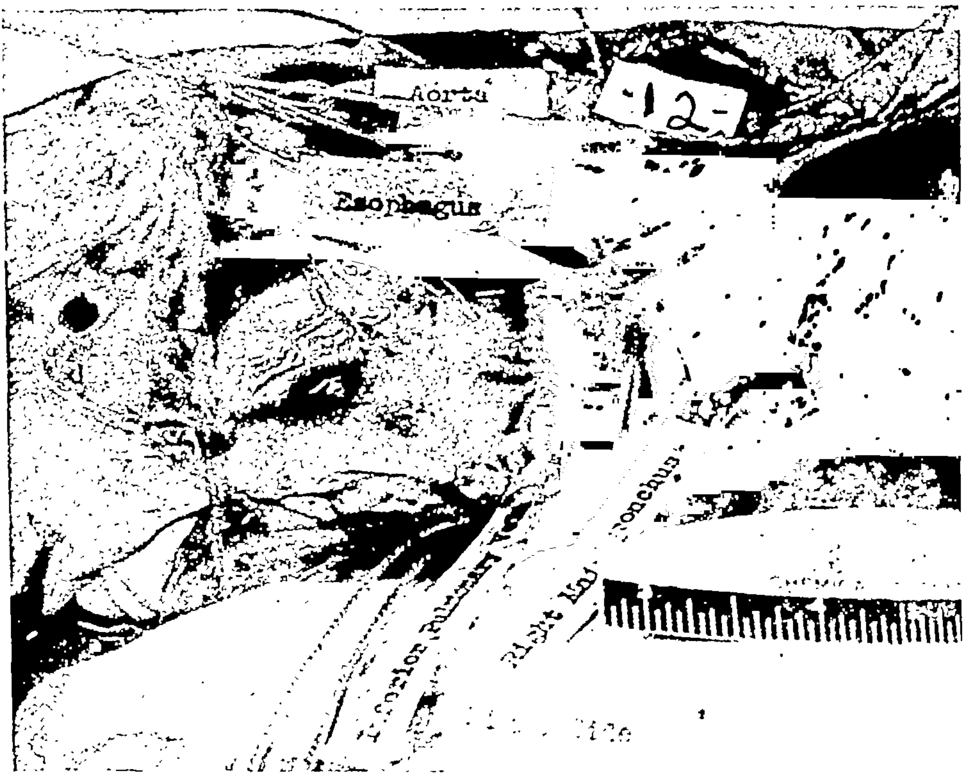

Fig. 2.—Appearance of the vagus nerve at the right pulmonary hilum.

It, of course, occurred to us that factors other than the operation might have been responsible for the relief. Accordingly, in 12 cases patients were subjected to avertin-ether anesthesia from one to four hours and allowed to recover from the effects of the anesthetic. In our series, the longest respite from an asthmatic attack was forty-eight hours.

The same precaution was taken concerning the effects of bronchoscopy on the asthmatic patient and again relief for more than a few days was not obtained.

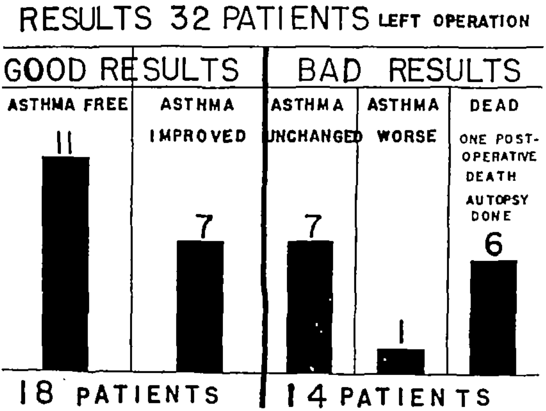

Fig. 3.—The results in 32 patients subjected to left pulmonary denervation.

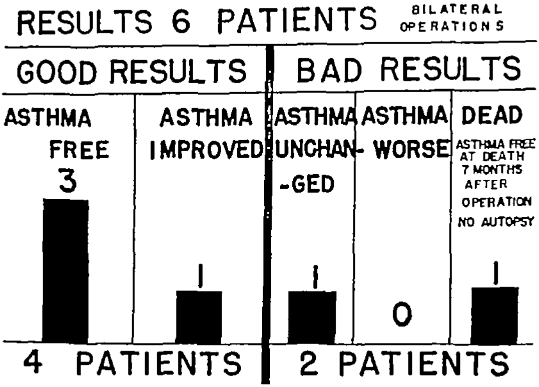

Fig. 4.—The results in six patients treated by bilateral pulmonary denervation.

Several methods have been employed in an attempt to find an objective test to estimate whether or not operative interference would be beneficial. Reactions to injections of adrenalin, aminophyllin, and other drugs have not, in our series, been useful in the selection of patients. In this connection it is important to record that more than 50 per cent of the cases were "adrenalin fast."

Studies of lung volume, including determinations of residual air, have offered no help in the selection of patients, but have been useful in evaluating the postoperative results. Attempts to obtain bronchospirometric readings have been abandoned because the patients have been so short of breath reliable data could not be obtained.

Results.—The results in 32 patients subjected to left-sided denervation are shown in Fig. 3. Of the 32 cases, 11 are free of asthma; 7 patients believe they are definitely improved; and in 7 the disease is unchanged. In 1 the asthma is worse. The categories of improved and worse, in our opinion, have little significance.

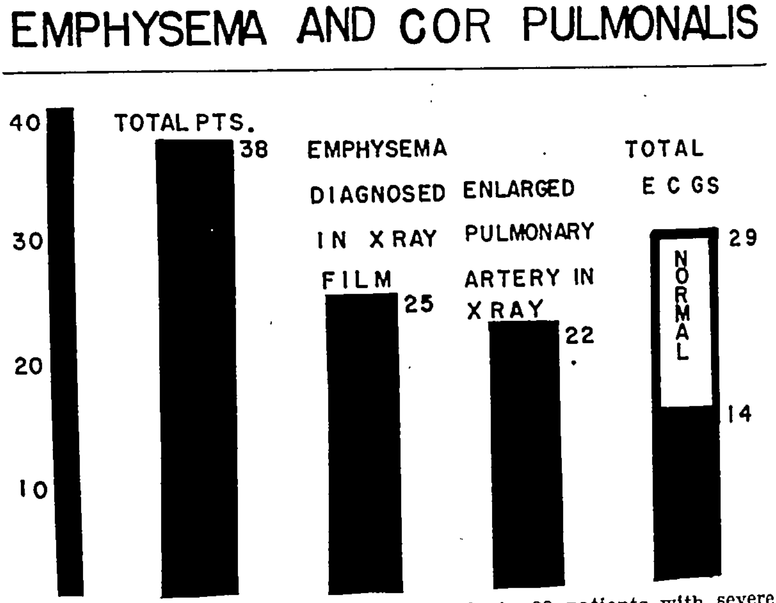

Fig. 5.—Incidence of emphysema and cor pulmonale in 38 patients with severe asthma.

In the entire series of 38 cases, there has been one operative death. This was in a man 73 years of age, who had suffered from severe asthma for many years and had far-advanced emphysema and cor pulmonale. He was in the hospital for some time and we were persuaded to undertake the operation because he had threatened to commit suicide if something was not tried in his case. The operation was tolerated well, but on the second postoperative day, while sitting in a chair having breakfast, he died suddenly. The post-mortem examination revealed a spontaneous pneumothorax on the right side; the left side had been operated upon. The remaining six deaths occurred at intervals from six to eighteen months following surgical intervention. The late mortality in this group of cases is not surprising when one considers the incidence of cor pulmonale and advanced emphysema in these patients.

The results in patients subjected to bilateral denervation are shown in Fig. 4. Three patients are free of asthma, one considers himself greatly improved and the disease is unchanged in one. The one death in this group was in a patient who was free of asthma for seven months after operation. He had cor pulmonale and severe emphysema and was found dead at home by his family. Permission for post-mortem examination could not be obtained.

Emphysema and Cor Pulmonale.—Fig. 5 demonstrates the incidence of emphysema and cor pulmonale in the group. A clinical impression of emphysema was not accepted and only in those patients in whom emphysema was obvious on roentgen examination was the diagnosis recorded. Cases included in the column labeled enlarged pulmonary arteries are those in which an unequivocal diagnosis of cor pulmonale could be made. These data make obvious the reasons for the late mortality in the group.

It is interesting and somewhat bewildering that relief of symptoms was effected in patients with emphysema in about the same proportion as in those without this complication.

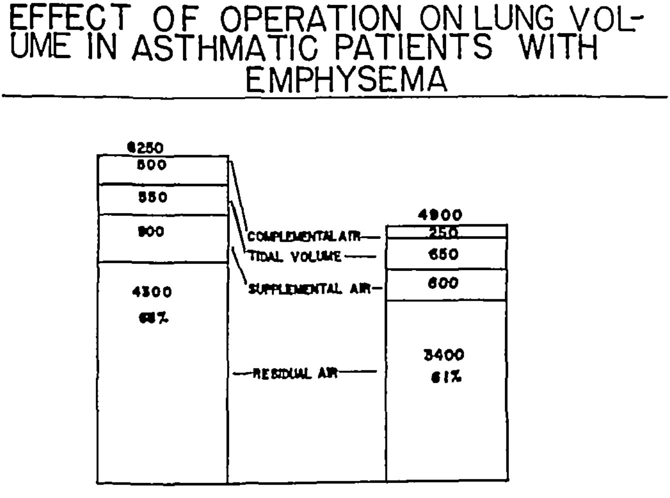

Fig. 6.—An example of lung volume studies in a patient with asthma and emphysema, before and after operation.

Lung Volume Studies.—Fifteen patients have been studied before and after operation with measurements of total lung volumes and the percentage of residual air, utilizing a helium spirometer modeled after the McMichael modification of the Christie method. A Sanborn spirometer and a helium-air analyzer manufactured by the Cambridge Company have been employed. Fig. 6 reveals the apparent effects of the operation on lung volume in a patient with severe asthma and emphysema. The interval between the preoperative and postoperative studies was eleven days. Temporary reduction in vital capacity is expected after any intrathoracic operation. Longer periods of observation and a larger series of patients will be required before definite conclusions on the effects on lung volumes can be accepted.

Pulmonary Artery Pressures.—Pulmonary artery pressure readings before and after operations in human subjects have been hampered by technical difficulties but will be accomplished in the future. The importance of these studies is suggested by observations made on dogs which have had bilateral

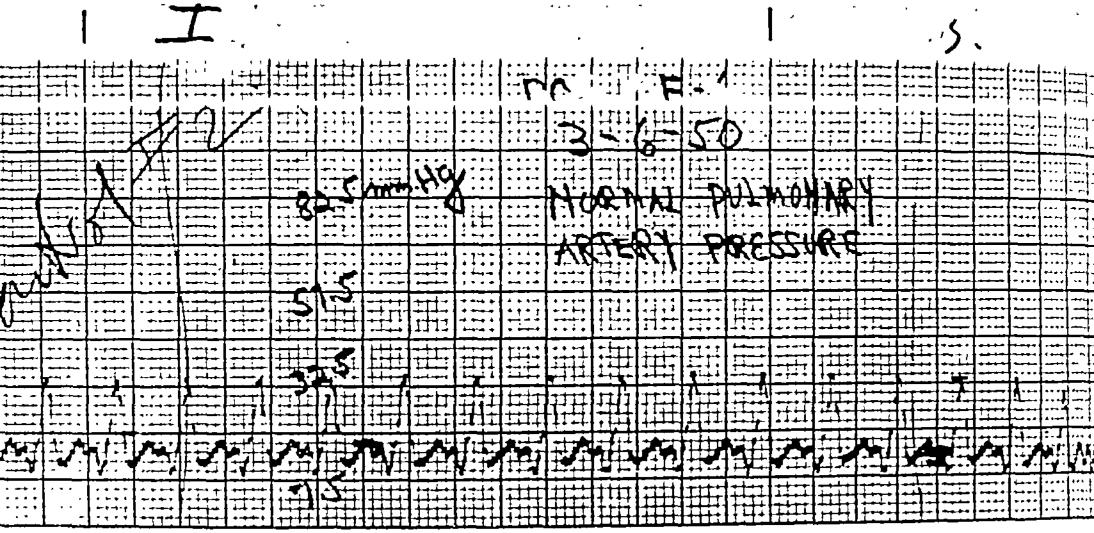

Fig. 7.—Pulmonary artery pressures in a normal dog.

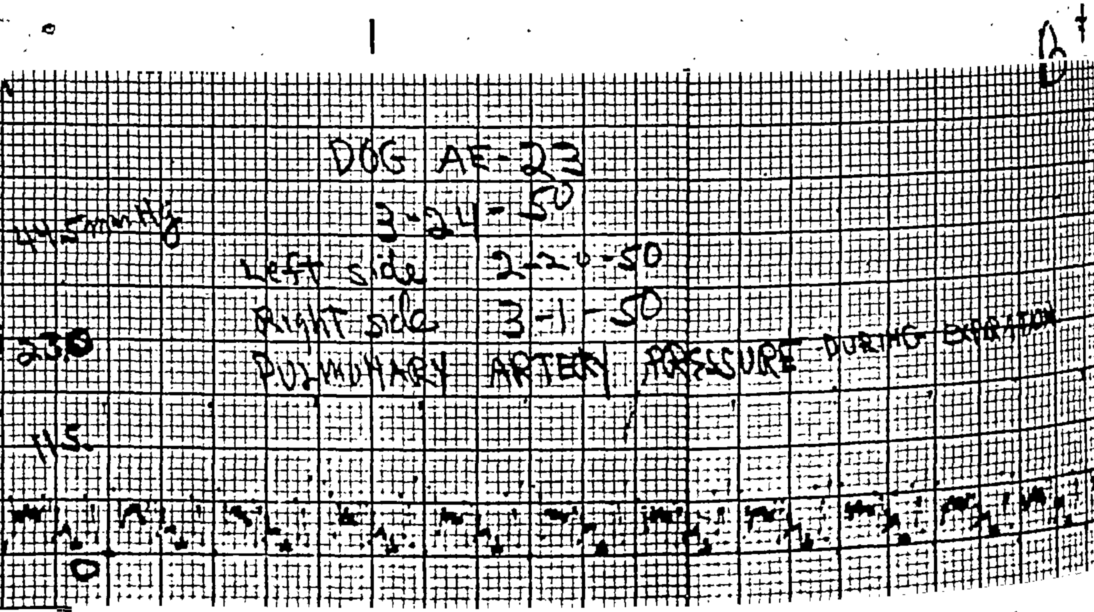

Fig. 8.—Pulmonary artery pressures in a dog following bilateral pulmonary denervation.

pulmonary denervations. Control animals were subjected to bilateral thoracotomies without interference to the nerve supply. The other series of dogs had bilateral denervations comparable to the operation which has been performed in the human being. Fig. 7 reveals normal pulmonary artery pressure readings in a control dog, of 32 mm. of mercury systolic pressure and 10 mm. of mercury diastolic. Fig. 8 demonstrates the pressure tracing on a dog subjected to bilateral pulmonary denervation. The pressures in this animal were 17 mm. of mercury systolic and 3 mm. of mercury diastolic. These changes in pressure are to be confirmed in the human being but the findings are suggestive.

Ramifications of attempts to study the functions of the vagus nerves include observations on tolerance to lycopodium spore injections in normal and denervated animals and observations on electrocardiographic tracings in both human beings and animals with extensive vagus nerve destruction. These will be reported in separate communications.

SUMMARY

A total of 38 patients have undergone surgical intervention for the treatment of intractable asthma. In 14 cases the patients are free of disease. Eight patients consider themselves improved. In 8 cases the disease is unchanged; and in one instance the asthma appears to be worse. There was one postoperative death and six late deaths.

These data demonstrate the bewildering consequences of an empirical surgical approach.

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DISCUSSION ON "A PHYSIOLOGIC EVALUATION OF VAGUS SECTION FOR BRONCHIAL ASTHMA" BY DR. KARL P. KLASSEN, DR. DOUGLAS R. MORTON, AND DR. GEORGE M. CURTIS;* "THERAPEUTIC STATUS OF PULMONARY AUTONOMIC NERVE SURGERY" BY DR. OSLER A. ABBOTT, DR. WILLIAM A. HOPKINS, AND DR. PAUL H. GUILFOIL;† AND "THE SURGICAL TREATMENT OF INTRACTABLE ASTHMA" BY DR. BRIAN BLADES, DR. EDWARD J. BEATTIE, JR., AND DR. WILLIAM S. ELIAS

DR. A. J. GRACE, London, Ontario.—This problem interested me first in 1945, and at the St. Louis meeting when Dr. Carr presented his paper on autonomic work along this line, I presented a brief survey of 11 cases, a very small series, which had been done in the preceding 15 months. Actually, that discussion did not find its way into the JOURNAL, for some reason, and I thought it might be worth while to bring up the clinical survey of those cases to date and to put that material in tabulated form. I am omitting further cases done more recently. There are a few; I have limited them strictly because of the

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*See page 552 for article by Klassen, Morton, and Curtis.

†See page 571 for article by Abbott, Hopkins, and Guilfoil.

FOLLOW-UP RESULTS: BILATERAL PULMONARY VAGAL DENERVATION FOR INTRACTABLE ASTHMA

PATIENT	AGE (YEARS)	SEX	DURATION DISEASE (YEARS)	OPERATIVE YEAR	RESULTS		DEAD
					EARLY	LATE	
A. I.	37	M	3	1946	Good	Good	—
R. J.	27	M	8	1946	Good	Good	—
M. R.	31	M	25	1946	Good	Good	—
H. S.	55	M	28	1946	Doubtful	Fair	—
E. W.	56	M	26	1946	Fair	Fair	—
F. S.	70	M	16	1946	Good	—	4 months
D. P.	24	M	15	1945	Fair	Poor	2 years
F. T.	35	F	10	1946	Fair	Poor	—
E. B.	44	M	7	1946	Poor	Poor	—
F. R.	50	M	27	1946	Poor	Poor	—
E. S.	51	F	3	1947	Poor	Poor	1½ years

confused state of our thinking and understanding of the basic physiology involved, and have felt that we should be forced into this procedure only for absolutely hopeless cases of the type described by Dr. Blades and our other associates.

This slide tabulates the essential data on 11 cases completed between November, 1945, and February, 1947, giving a follow-up period exceeding three years in all patients. The age and sex of each patient are listed along with the duration of disabling asthma The operation was a fairly radical type of resection of every demonstrable vagal connection on both sides, done in two stages. An attempt has been made to evaluate the status of each individual in relation to the passage of time. I wish to emphasize the fact that some patients failed to maintain initial improvement, while one patient in particular seemed to gain steadily with the passing years, after a disappointing immediate response. In general, I am not happy about the results in the older age groups, although the man 70 years of age seemed most successful until his early death on a cardiac basis.

In this very limited series the only striking results were shown by the first three, relatively young men; each of these has been restored sufficiently to hold down a full-time job satisfactorily, something which was absolutely impossible before operation. These cases encourage one, but I am not at all sure that even they are in any sense "cured" of their asthma. They are free from any gross disability.

As stressed by Dr. Blades and others, we must be very careful in assessing "results" after any operative procedure for asthma. The time factor must receive consideration along with many other variables. The entire problem calls for much more investigation.

DR. ROBERT P. GLOVER, Philadelphia.—Our results with complete denervation of the lung, at least our understanding of complete denervation of the lung, carried over a two-year period, are summarized on the first slide. Our operative approach is to remove or resect segments of all the branches of the vagus nerve on the left side and the right side, from the recurrent laryngeal nerve down. We do not transect the main trunk of the vagus nerve. We also carry out a circumcisional denudation of an area about one inch along the course of the bronchus, the pulmonary artery and the pulmonary veins, and remove or detach the inferior pulmonary ligament. This has been carried on for a period of two years.

We were stimulated in this work by the work of Carr and of Blades. We have carried out a unilateral procedure on the left side in 25 cases and a bilateral procedure in 4 cases. Five of these patients are now asymptomatic; 6 others we consider to be improved; their trouble at present is concerned with secretions and not with asthma per se. There are 18 unimproved cases, including four deaths; two of the latter were operative, two have since died in what appeared to be status asthmaticus. Two of the unimproved cases had the major bronchus completely transected and then repaired; it did not seem to improve the result. Four other cases had removal of the sympathetic ganglia from the second to the fifth thoracic vertebrae also without improvement; one of these was bilateral. All these cases have been followed to date. As a matter of fact, we are having difficulty in some instances in losing the patients, particularly those who are still having trouble. Sections removed from the lung in one-half the cases have been examined pathologically, and in only one was there evidence of emphysema.

DR. LAWRENCE MISCALL, New York.—In 1942, we reported 21 cases upon which we had done some form of sympathectomy for intractable asthma. These were patients who crowded the Bellevue Clinic. They had run through the gamut of all medical care but they were there daily. We tried to select patients for surgery in this way: the medical service had turned them over as being unaided by anything they could offer. We took patients who had not been treated for an extended period of time in the allergy clinic; most had been labeled as intractable asthma on a recurrent infectional basis. We were prompted to attack from the sympathetic side rather than posterior pulmonary plexus resection because of the experience of Rienhoff. We selected patients for operation only after they had been benefited by a stellate block. Of 61 patients whom we blocked we were able to obtain variable relief in 47, or 78 per cent. Of this group we accepted 21 patients for operation because of a definite improvement after block, which was not maintained. In 1942, we had followed them for from two months to two years. We were greatly impressed with the group. We thought we had the method by which we could select those who would be benefited by operation for a long period of time.

The war came along and the work was suspended. Since the war we have been able to follow 11 of these patients; 6 have had good results; the others have had miserable failures, which is about a 50 per cent failure rate. Since that time we have been doing a much more widespread operation; resection, bilaterally, of the upper dorsal chain and a parasympathetic denervation. Our results are still no better. We can obtain only about 50 per cent cures. I think this depends upon what one considers a cure. The only ones we have accepted are patients who do not come back to the Clinic routinely. I think the solution of the asthma problem is going to come when we are able to define a disease and not be treating a symptom complex.

DR. RALPH ADAMS, Woodbury, Tenn.—One may further confound confusion by a report on 21 patients, the last one operated on more than a year ago, all of whom at this time have proved to be failures. Some of these cases were reported following Dr. Carr's report; some of those, as some of the cases reported this morning, were brilliant early successes and led us to perform further operations upon additional patients. The problem at this time seems to me to be similar to that of removal of the thymus gland for myasthenia gravis uncomplicated by tumor; follow them long enough and they will again have myasthenia gravis; as the asthmatics will again have asthma.

In the section of the country where I live, financial considerations are of greater importance than in some sections where I have lived. It was of interest to determine the cost to the patient in a group of eight of these denervations for asthma. The cost of hospitalization, for these patients having bilateral combined extensive sympathetic and parasympathetic denervations, as I understand it, was slightly over $500 per patient. In the end, these patients, if they are still alive without having died from a recurrent attack of status asthmaticus, have had no more than a term of symptomatic improvement from operation. That amount of money will buy a great deal of aminophyllin or adrenalin.

DR. DUANE CARR, Memphis, Tenn.—I, too, am from the low income section of the country. From the excellent presentations that have been given, it becomes apparent that a certain number of patients with previously intractable asthma are definitely benefited by any one of the various surgical attacks upon the autonomic nervous system. But the wide variation in results obtained indicates that none of the procedures strikes at the root of the trouble.

It so happens that we favor the dorsal sympathetic ganglionectomy because it is so cheap; at least it involves less surgery than the more radical transpleural operations and is therefore better tolerated by some of these extremely ill patients, and we believe this operation gets away from the postoperative pulmonary function restrictions which do occur following a transpleural operation. The results obtained are not materially different from those reported following more radical procedures.

I believe it becomes apparent to everyone that there must be in asthma some basic, fundamental, underlying disease of the autonomic nervous system. Asthma is but one manifestation of it, and is perhaps closely related to other degenerative diseases such as hypertension. It has been a common finding that in each ganglion removed for the treatment of asthma degenerative change has been found. This is not only our observation but that of others.

In addition, we must know something more about the modus operandi of asthma. It has not been proved by anyone that bronchial spasm actually exists; a simple demonstration of diminution of bronchial caliber does not necessarily mean bronchial spasm. There is not one whit of evidence to show that bronchial muscles contract to throw the patient into an asthmatic attack, any more than there is to indicate that the nasal bones contract when one has an attack of hay fever. We do know that changes in the bronchial mucous membranes occur as a result of numerous stimuli, such as direct contact with allergens, changes in temperature, emotion, infection, and a host of others which do *not* produce asthma in a *normal individual.*

We are impressed with the way asthma disappears in the youngster as he reaches the age of puberty, and the improvement in asthma as a result of the demand stimuli of an operation. It occurs to us that a fruitful field of investigation is the determination of the pathologic changes occurring in the autonomic nervous system in asthma, and in its governing hormone producing organs. Every patient dying of status asthmaticus, or who has been a chronic asthmatic, should at autopsy have a meticulous microscopic examination of the autonomic nerves and ganglia, and of the hypophysis and adrenal cortex at least. Until we learn what the basic pathologic and pathophysiologic action in asthma is, our treatment by attacks on the autonomic nervous system will be empirical, and all medical treatment will be no more than symptomatic.

DR. H. J. STANFORD, Tucson.—I should like to add to the comments of Dr. Adams and Dr. Carr, that perhaps our approach to the treatment of bronchial asthma is not exactly in the right direction. My own early enthusiasm following some highly satisfactory results has been dampened by later failures. This does not mean that we should discard surgical treatment. However, I can best illustrate the need for further study by giving the case history of one patient.

This man was first treated for involutional melancholia back east and received electric shock therapy. He improved and went back to work as a factory executive. One year later he developed intractable bronchial asthma and went through the gamut of treatment for this condition. He had severe asthma for the next five years, requiring repeated hospitalization. About six months ago, I found on bronchoscopy that he had marked bilateral bronchial spasm and blockage of the bronchi with inspissated mucus and bronchial casts. Following this, I did a right-sided pulmonary denervation that included the sympathetic chain down to the sixth thoracic, the posterior pulmonary plexus, and stripping the pulmonary artery.

During the first three postoperative days there was no improvement. From the fourth day on he had complete cessation of his asthma which lasted for five weeks. After this his asthma returned and, in addition, he went into a manic psychosis state. The psychiatric consultant called in advised shock therapy. He was flown back east, where he received a series of electric shock treatments with no improvement. He was next given a course of ACTH therapy for ten days. This was more than two months ago. He had an immediate remarkable cessation of all his symptoms, is back at work, and has had no asthmatic attacks to date. The result of the therapy with ACTH is what I wish to emphasize, because it points to a possible new approach to the entire problem of cause and treatment of bronchial asthma.

DR. J. H. WALKER, Boston.—We have been doing surgery at the Overholt Thoracic Clinic for bronchial asthma for two years. We have studied this group of patients through sympathetic blocks and bronchography, and it has been most interesting to us to find that 40 per cent of our 25 patients have had some type of abnormal localized pathology that has needed resection. Thirty-five per cent of our patients have responded to sympathetic block and have had sympathetic surgery. We have noted improvement in about two-thirds of these. Three of these patients had only one lung, one was congenital and two from pneumonectomy eight to ten years ago; two of these patients have had dramatic results.

It is interesting that none of the cases treated with sympathectomy, or that responded to a block, have had any localized pulmonary pathology. Cases that we have treated by pulmonary neurectomy and excision of diseased pulmonary tissue have given the best results. *We have noted improvement in about 75 per cent of them, and it has been a* most satisfactory type of improvement. I want to repeat, that his has been done only for a period of two years.

DR. EMILE HOLMAN, San Francisco.—We are indeed indebted to those various authors for bringing us up to date on the surgical efforts to cure this intractable disease. I am wondering, however, if we are not on the verge of a new era in treatment of this disease, as suggested by one of the preceding speakers. A member of our faculty has for thirteen years injected himself every two to three hours, night and day, with epinephrine for bronchial asthma. In periods of stress, as during a lecture, he has injected himself as often as every thirty minutes. On March 7, 1950, he entered the hospital in a state of severe asthma; intravenous aminophyllin failed, and epinephrine no longer produced the same effects as formerly. He had marked pulmonary edema. On March 7, he received 100 mg. of Cortisone intramuscularly; on March 10, he said he felt better than he had in five years, and gleefully reported that he had injected himself only four times in the preceding night. The Cortisone was dropped on March 13, to 33 mg., and he is now on a daily maintenance dose of 25 mg. of Cortisone, and is completely free of asthma.

DR. GEORGE M. CURTIS, Columbus, Ohio.—Our studies have been made in an attempt to find something helpful concerning the clinical physiology of the human tracheobronchial tree. And, consequently, intractable asthma, widely thought to be a manifestation of smooth muscle spasm, has become a part of our observation.

Five features of the neurophysiology of the human bronchi have come under this consideration; the *first*, the sensory nerve supply of the tracheobronchial tree. This has been fairly well worked out from the standpoint of the anatomist; however, it needs better clinical application. It has become apparent that pain of tracheobronchial origin is carried to the central nervous system largely through the vagus. The cough reflex is initiated and the resultant impulses are carried to the central nervous system mainly by means of the vagus. These are our two most useful clinical findings thus far.

The *second* has to do with the motor activity of the smooth muscle in the tracheobronchial tree. There is a definite band between the ends of the horseshoe formed by the tracheal rings. There are definite sheaths around the bronchioles. It is difficult to dissociate smooth muscle from the clinical picture of intractable asthma, even if we consider, as Dr. Holman has suggested, the existence of a hormonal mechanism. The motor control of this smooth muscle appears to an extent through the vagus. In fact, the vagus has been termed the "pulmonary motor nerve." On the other hand, our studies on bronchial asthma appear to show that after bilateral vagus section there remains spasm of the bronchial smooth muscle.

Our *third* approach has concerned the secretory activity of the bronchi and of the trachea. There are two types of secretion: the first, from the goblet cells in the epithelium;

the second, from the bronchial glands, which are mixed glands and therefore may at times form a thick, more mucoid secretion; or at other times, a more watery fluid. The nerve control of bronchial secretion thus becomes important. It is questionable, however, how much nerve control exists over the goblet cell.

Our *fourth* point has to do with ciliary activity. This is of considerable significance. Thus, in the discussion this morning we heard that if high vagotomy is done the patient may develop a wet lung. One might think that this could be due to inadequacy of the cilia. Ciliary movement is one of the oldest forms of movement, next to amoeboid. There is no apparent connection between the nervous system and ciliary activity.

The *fifth* factor has to do with the causation of edema of the bronchial mucosa. Edema may be precipitated by psychosomatic factors. Therefore there is possible an effect from the central nervous system.

We have approached the problem through these five avenues, from the standpoint of useful clinical physiology. However, thus far we have not the solution of intractable asthma, since we feel the same as others who have expressed themselves this morning.

DR. E. A. GAENSLER, Mattapan, Mass.—Objective physiologic evaluation of patients with bronchial asthma before and after surgery for its relief are of the utmost importance. Only results of such laboratory studies will eventually show various surgical procedures in their proper light. In conjunction with a preoperative medical and psychiatric evaluation, such physiologic studies should be expected to do three things: (1) aid in ruling out a number of patients whose respiratory difficulty is due to causes other than bronchial asthma; (2) give an early indication between and after surgical stages of the results of such surgery; and (3) formulate a set of physiologic findings and responses which, after some experience, will aid in the preoperative prediction of the likelihood of success of surgery.

A number of interesting and valuable objective observations for the study of asthma have been described this morning. We presume to add a number of suggestions derived from our experience in the study of more than 120 patients with varying degrees of bronchial asthma and pulmonary emphysema, only because the number of patients with asthma of sufficient severity to warrant surgery is at the present time small, and we feel that an earlier and better evaluation of such surgery will be possible if more and better tests before and after surgery are used for the evaluation of results.

Vital capacity determinations are not only unreliable in the presence of bronchospasm and/or loss of pulmonary elasticity, but also give a false impression of the degree of pulmonary insufficiency present. The maximum breathing capacity is the single most valuable test except in those patients where attacks of asthma are elicited by this test. Studies of patients with bronchial asthma could not be carried out on one or two occasions, but patients should come to the laboratory at scheduled repeated time intervals, and identical tests should be repeated at weekly or biweekly intervals for at least four to eight weeks, in order to give the patient an opportunity to become acquainted with the laboratory staff and the testing devices. Only such repeated studies can possibly lead to a relatively good base line in asthmatic patients where functional results often vary a great deal more with home and business conditions than with medical or surgical therapy. Tests should be repeated not only after the administration of bronchodilator substances but also after artificial induction of asthma by intravenous injection of histamine and methacholine, as outlined by Curry and Lowell and Segal and Beakey. Preoperative responses to one or the other drug may eventually give a clue as to good prospective surgical candidates. Bronchospirometry before, between, and after surgical stages has been found of great value, particularly if asthmatic attacks are induced as outlined above, during the course of the procedure. Finally, pneumatographic studies between and during attacks aid in the measurement of inspiratory-expiratory time ratios and air flow velocities.

A small number of patients studied by us in this manner during and after surgery have all had bilateral vagectomy below the recurrent laryngeal nerve, and posterior pulmonary plexus resections—operations carried out by Dr. John W. Strieder and Dr. Dwight E. Harken.

No conclusions can be drawn at this time, but three observations may be recorded here. Unilateral operations have been found to be of no value. Patients with advanced pulmonary emphysema, secondary to long-standing bronchial asthma as evidenced by poor bronchodilator and bronchoconstrictor response, persistently large residual air values and persistent low arterial oxygen tensions and high carbon dioxide tensions after exercise, have not benefited by such surgery. Interruption of the innervation of the lungs cannot be expected to repair lungs with permanent and irreversible anatomic destruction and disruption. And, last, there is good evidence obtained during bronchospirometry with artificially induced asthma, that occasional patients have predominantly unilateral asthma in the absence of unilateral anatomic disease.

DR. MORTON (Closing).—This discussion has been quite prolonged, so I merely wish to thank the men who have participated.

DR. ABBOTT (closing).—The lack of satisfactory results in the presence of diffuse suppurative disease or in cases with nonresectable amounts of pulmonary destruction should be stressed. I suspect that after a certain duration of disease, results from complete plexectomy are less satisfactory. The loss of ciliary function in long-standing bronchial asthma is well known. We feel that with proper selection of patients, pulmonary denervation will find its proper place in the treatment of bronchial asthma.

DR. BLADES (closing).—It seems to me the principal accomplishment of this morning's discussion has been to stimulate interest in the surgical treatment of asthma.

The costs of hospitalization in Tennessee are amazing. In my opinion, a $500 purchase of adrenalin for the adrenalin-fast patient is as poor an investment as $500 spent for hospitalization without good results.

The presence or absence of bronchial constriction cannot, in my opinion, be determined accurately either by bronchograms or bronchoscopic examinations. Dr. Holman's comments on the use of Cortisone in the treatment of asthma are interesting. The availability of this drug may change the whole problem in the treatment of asthma and make surgical intervention completely undesirable.

The psychogenic factor in asthma has been mentioned. This is well known, and perhaps if these patients were subjected to prefrontal lobotomy they might still have asthma but would not care. This important aspect of the disease is one of the many imponderables of the question.

THE EXPERIMENTAL USE OF HOMOGENOUS TRACHEAL TRANSPLANTS IN THE RESTORATION OF CONTINUITY OF THE TRACHEOBRONCHIAL TREE

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INTRODUCTION

THE rapid advances in surgery of the thoracic viscera which have occurred during these last twenty-five years have made healing and regeneration of tissue within the tracheobronchial tree of significant practical importance. Taffel,[1] in 1940, reported the use of fascia in the repair of small tracheal defects in dogs. Daniel,[2] in 1948, reported experiments in which rigid tubes were used to bridge defects in the trachea and the primary bronchi. He discussed in detail the growth of the tracheobronchial wall in relation to these rigid tubes. Hanlon,[3] in 1948, reported his observations in dogs, where gelatin sponge was used in the closure of defects of the bronchus. Jackson and associates[4] published experiments in 1949 observing the results of end-to-end anastomosis of the bronchi following resections of segments of the primary bronchus. They found this could be performed successfully in dogs without significant morbidity to the lung or bronchus either functionally or anatomically and described a technique in detail.

However, the problem posed in the bridging of extensive defects of the trachea and bronchus where end-to-end anastomosis is not feasible presents a stimulating challenge. Ideally one must construct a tube in the tracheobronchial system that will remain at least semirigid, and will become an integral part of that system permanently allowing for the passage of air and secretions. Should one pursue successfully this endeavor, then the discouraging problem of extensive destructive lesions of the trachea and possibly tracheobronchial segments, would lend itself to surgical treatment.

One of us (E. J. O'B.) became intensely interested in this subject after reviewing the recent work of Gebauer. The latter[5] published work in 1949 in which plastic repair of bronchial stenoses was accomplished by using skin grafts which were held rigid by the interlacing of wire sutures. After discussions with Gebauer, we were led to attempt experiments to restore the tracheal continuity using living and preserved tracheal grafts.

HISTORICAL REVIEW OF TRANSPLANTATION

The study of tissue transplantation is not new to this decade. Anatomists and physiologists have long maintained such an interest and speculated on its practical possi-

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From the Department of Surgery, Harper Hospital.

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bilities. Probably one of the first experiments to be performed on the grafting of cutaneous tissue, can be found in the writings of John Hunter (1794) and is here related in his own words.

"I took the spur from the leg of a young cock, and placed it in the situation of the spur in the leg of a hen chicken; it took root, the chicken grew to a hen, but at first no spur grew, while the spur that was left on the other leg of the cock grew as usual. This experiment I have repeated several times in the same summer, with the same effects, which led me to conceive that the spur of a cock would not grow upon a hen and that they were, therefore, to be considered as distinct animals, having, very distinct powers. In order to ascertain this, I took the spurs of hen chickens and placed them on the legs of young cocks. I found that those that took root grew nearly as fast and to as large a size as the natural spur on the other leg."[6]

Hunter was also a strong advocate of transplantation of teeth from one person to another. This, a prevalent practice in his day, soon fell into disrepute. To quote Hunter:

"The scion tooth, or that which is to be transplanted, should be a full grown young tooth; young, because the principle of life and union is much stronger in such than in old ones. . . . The new teeth should always be perfectly sound, and taken from a mouth which has the appearance of that of a person sound and healthy."[7]

Time has shown that his views on the viability of grafted teeth were largely erroneous (Colyer,[8] 1913). His work is of great historical interest and demonstrates the tremendous scientific vitality with which he was gifted.

It is of note, that in Hunter's time, in Europe as well as America, high prices were offered for teeth for transplantation. Taylor,[9] in his *History of Dentistry*, noted a newspaper advertisement in 1782 offering four guineas for each sound front tooth. A dentist by the name of Jullion charged a fee of five guineas for transplanting a live tooth and two guineas for dead ones. One also remembers the account of the girl Fantine in *Les Miserables*, who offers the sale of her teeth to provide money for the care of her child.

In the development of tissue transplanting, the use of skin has always been of major interest. In this paper we are only concerned with the problem of the transplanting of tissue from one individual to another of the same species. To date it can be stated that the success of homogenous transplants of skin is unsettled, questionable, and opinions are widely divergent. Early workers claimed success. Such is expressed by Oshima[11] in 1914. Lexer,[12] in 1911, had no success at all. Masson,[13] in 1918; Dyke,[14] in 1922, believed that the success of homoio-skin grafts depended on blood compatability of donor and recipient.

Dobrzaniecki,[15] in *1920, thought that except between uniovular twins, such grafts are* never permanently successful, though survival is prolonged by identical blood grouping. Trusler and Cogswell,[16] in 1935, believed that though such grafts may at first adhere well and appear to have taken, they always slough later.

Willis,[10] in 1939, delivering the Victorian Lecture (University of Melbourne), presented a comprehensive review of tissue transplantation and its relationship to surgery. His summary of homeotransplantation included numerous tissue types, embryonic as well as adult. He felt that generally in all homeotransplantations, there was not a permanent growth of the graft, as such. Says he of bone: "to me the evidence suggests that, on the one hand the greater bulk of a large bone graft (homogenous) dies and is replaced, but in suitably small fragments parts survive and contribute to osteogenic repair."

Attempts to treat Addison's disease by transplantation of adrenal tissue from other people or fresh corpses have been reported with temporary benefit. Hurst,[17] in 1922, Pybus,[18] in 1924, and Beer,[19] in 1934 reported such cases.

Other reports are found in reference to transplantation of ovary, testes, and pancreas, but no proved permanent result is maintained. A group of German scientists became intensely interested in the problem in the decade 1920 to 1930 and made numerous investigations. Gins,[20] in 1927, discussed the failure of epithelial cells to survive in transplanted tissue. His observations were concerned with the lack of stimulus to growth and the autolysis due to formation of lysing tissue juices. Baetzner and Beck[21] discussed the problem of ''homeotransplantation'' in 1928, and reported the failure of these tissues to retain their individuality in the host. Similar studies were published by Fischer[23] in 1929. Bruda,[22] in 1930, attempted to show the relationship between the success of homeoplastic grafting and the reticulo-endothelial system. Ruditskiy,[24] in 1936, conducted similar investigations.

The important biochemical factors preventing growth of grafts was discussed by Loeb and Addison[25] in 1909. This effect was felt to be less in autogenous and strongest in heterogenous transplanting. They felt the tissue fluids of the host have a harmful effect on the transplanted structure. The closer the relationship to the host tissue, the more chance the cells have to live. Loeb declared that dissimilarity between two tissues leads to the development of heterotoxins which are directly responsible for the reaction on the part of connective tissue and lymphocytes in the host tissue, as well as interference with vascularization.

Loeb,[26] in 1908, from experimental work concluded that there exists a difference between the adequacy of the different species as a soil for epithelium, and that the more nearly related two species are, the better will be the growth of epithelium.

Most of these factors are eliminated with the use of preserved transplants however, since the cells are not viable. One must depend on the growth of connective tissue, epithelium, and other forms, from the surrounding host tissue. Weiner,[27] in 1943, discussed the use of preserved grafts and transplanted the conjunctiva of the cow to the eye of the rabbit with some success. His transplants were formalinized.

Greene,[28] in 1943, found that embryonic mammalian tissues could be grown in adult alien species and that such transfer was readily effected as homologous embryonic transfer. Willis,[10] in his report, found embryonic tissue more adaptable. Greene,[29] in 1945, reported the production of carcinoma and sarcoma in transplanted embryonic tissue treated with methylcholanthrene. He postulated that the reserve stem or partially differentiated cells of the body formed the source of neoplastic cells in adult animals.

Sheehan,[30] in 1943, discussed various types of tissue grafting and advised the removal of the perichondrium from autogenous and homogenous cartilage grafts. He felt this essential to the success of the grafting.

Algeri,[31] in 1945, ingeniously using transparent chambers inserted in skin flaps in mice, described the vascular reaction to tissue transplants. He reported the early accumulation of fluid and leucocytes followed by a rapid and dense vascularization, thence by scar tissue growth. In tumor transplants he declared the outstanding characteristic of the neoplastic cell to be its capacity to elicit continued growth of new capillary endothelium from the host which was sharply different from the reaction to normal tissue and an expression of neoplastic change.

With regard to the clinical use of autogenous transplants, Neuhoff[32] reported in 1941 the successful use of a fat mass removed from above the iliac crest to close a pulmonary cavity with bronchial fistula.

Harrison,[33] in 1936, reported a case of tracheal stricture following attempted suicide. He removed the stricture and placed a Thiersch skin graft over the raw surface. A successful recovery followed.

Negus,[34] in 1938, reported the use of thin autogenous skin grafts over the vocal cords to prevent their adherence after surgical separation. He also used skin flaps to reconstruct the continuity of the laryngotracheal segment in cases of fistula following irradiation.

Swinburne,[35] in 1941, discussed in detail the problem of laryngotracheal stenosis and the successful use of thin skin grafts in their plastic repair.

Nach,[34] in 1943, discussing methods in the closure of tracheal defects, made reference to the use of free fascia. He described the new tracheal wall following this grafting as composed of:

1. A layer of pseudostratified epithelium.
2. A layer of submucosa with occasional mucous glands, a few small islands of new cartilage, but with occasional exceptions, no fibers of muscularis mucosa.
3. An outer layer of supporting adult connective tissue.

From this summary one can say with few exceptions, that adult homogeneous grafts give no permanent structure in tissue grafting. There is some indication that embryonic tissue may be more successful. Fresh homeotransplants meet a great resistance in the host, with resultant liquefaction. This is principally due to the biochemical reactions set up in the host. Preserved grafts are not viable and do not excite so severe a reaction. When transplanted, they act as a superstructure, are absorbed, and in the case of the trachea, the end result of the tissue wall may be as described by Nach[34] (three layers as described in the preceding paragraph).

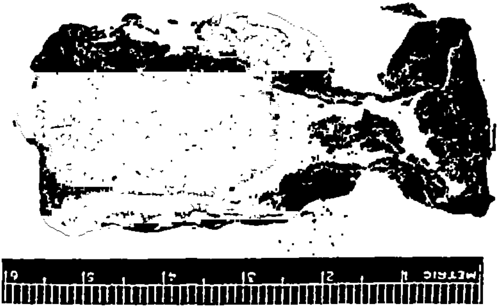

Fig. 1.—Massive liquefaction and death in 10 days with use of a fresh, viable, homogenous transplant.

It was desired by the authors to explore the possibilities experimentally, of bridging varying lengths of produced defects in the tracheobronchial tree of dogs, making use of homogenous tracheal transplants. The experiments were divided into two groups for evaluation and study.

Group 1.—Repair of small defects in the trachea and bronchus using homogenous transplants.

Group 2.—Resection of complete segments of the trachea up to two inches in length and closure with homogenous transplants.

METHODS

Eighteen dogs of nonspecific pedigree were used. Numerous others were used in standardizing the procedures and in setting up the program for study. Surgical procedures were performed under intravenous Nembutal anesthesia. For the cases in which the pleural cavity was entered (gaining access to the bronchus) oxygen was given by intermittent insufflation, making use of an endotracheal tube.

Preparation of the Transplants.—Early in the experiments several dogs were used to test and to standardize the type of transplant to be used. Two dogs of approximately the same weight were simultaneously anesthetized and complete one-inch segments removed from the trachea through a midline neck incision. The tracheal segments removed were transplanted from one dog to the other, using a simple end-to-end anastomosis of 0000 silk. The tracheobronchial tree was aspirated and the dogs given 100,000 units of penicillin daily. For the first four days, the postoperative course was not unusual. The animals walked out into the runway and ate regularly. However, they then began to stop eating and began to cough. Within ten days they presented signs of definite tracheal obstruction; they were weak, ill, and died rapidly. Fig. 1 presents the autopsy appearance of such a specimen. Gross section presented the picture of severe edema and liquefaction of the transplant with complete collapse of that portion of the trachea. Microscopic section as shown in Fig. 2, revealed edema, autolysis of tissue, with little evidence of viability or of ingrowth of connective tissue.

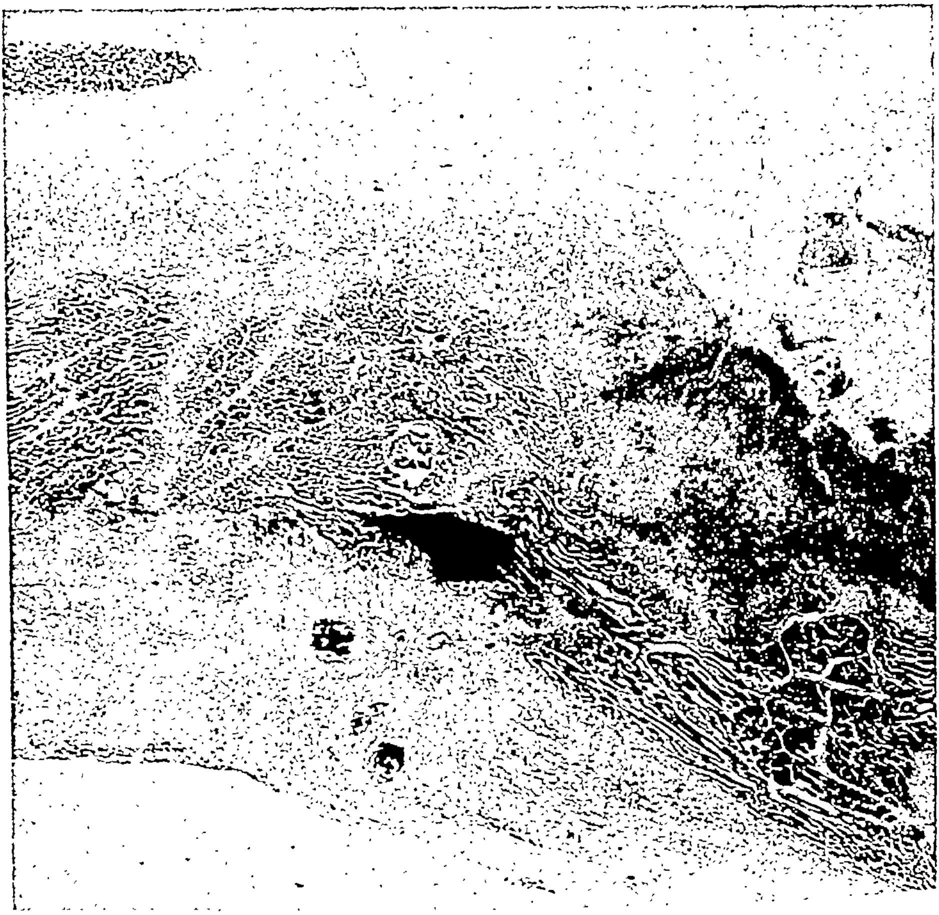

Fig. 2.—Section with low magnification, through the wall of the specimen seen in Fig. 1. Edema, necrosis, with no evidence of replacement.

Gins[20] had described this effect as due to the death of epithelium and the liberation of lytic enzymes. Silverberg and Voit,[37] in 1932, discussed the occurrence of thymonucleic acid in transplanted tissues, suggesting it as a factor. Cain,[38] in 1943, recognizing the problem of coagulation necrosis suffered by tissue transplants, felt it due to enzymes and reported the use of oxalate and enzyme poisons, to inhibit this sequence of events.

This coagulation and liquefaction of our transplants was anticipated. A preserved transplant was then decided upon, from which as much of the mucosa as possible and adherent peritracheal tissue had been removed. It was felt this transplant would offer purely a superstructure for the ingrowth of respiratory epithelium, connective tissue, and possibly cartilage. Also, this type of graft was nonviable, would cause much less severe local tissue reaction in the host, and present a greater chance for successful use.

A dog was anesthetized and the trachea removed under aseptic conditions. The membranous portion of the trachea was completely removed and as much as possible of the mucosa from the cartilagenous portion. The thin layer of vascular and connective tissue intimately adherent to the outer surface was removed. This, in effect, left only the cartilage of the trachea supported by the perichondrium and intercartilagenous fibromuscular framework. Fig. 3 represents such a graft. The specimen was then placed in a solution containing equal parts of sterile saline and aqueous Merthiolate. To this was added 500,000 units of aqueous penicillin. After refrigeration for twenty-four hours sterile cultures were obtained from the solutions in two-thirds of the cases. The specimens were replaced in fresh solutions and allowed to remain refrigerated for another twenty-four hours. The solutions were then uniformly sterile. The solutions were brought slowly up to room temperature before culturing. If the trachea was to be kept longer before use, *as a transplant, it was placed in a third fresh solution and placed in the deep freeze,* where it became suspended in a block of ice.

Fig. 3.—Homogenous, preserved, tracheal transplant that has been partially de-epithelialized.

The transplants were preserved in the solutions for two reasons.

1. The washing and dilution effect on the bacteria present.
2. The washing and dilution effect on the enzymes present.

The transplants were used at time intervals up to three weeks. The interval difference up to this length of time seemed to have no bearing on the success or failure of the transplant.

Standardization of Surgical Procedure.—A number of dogs were used before arriving at a practical and workable method of securing the transplants in place in the host. At first, simple end-to-end anastomoses of the graft to the trachea were performed. These dogs began to present symptoms of tracheal obstruction around the tenth to fourteenh days. Tracheoscopy revealed the grafted portion to be edematous and tortuous, and the lumen to be angulated at both suture lines. The rigid ends of the trachea of the host seemed to exert a hinge effect on the softer graft. It was felt that during this early period, when the sutures no longer held the graft tightly, any movements of the neck or filling of the esophagus tended to displace the transplanted portion off the direct line of tracheal continuity. Such a situation was abetted by the softening of the graft. Therefore a different type of anastomosis was instituted. To overcome to some extent the hinge effect a "sleeve" type anastomosis was performed as illustrated in Fig. 4. This type of anastomosis was used in all the dogs in Group 2.

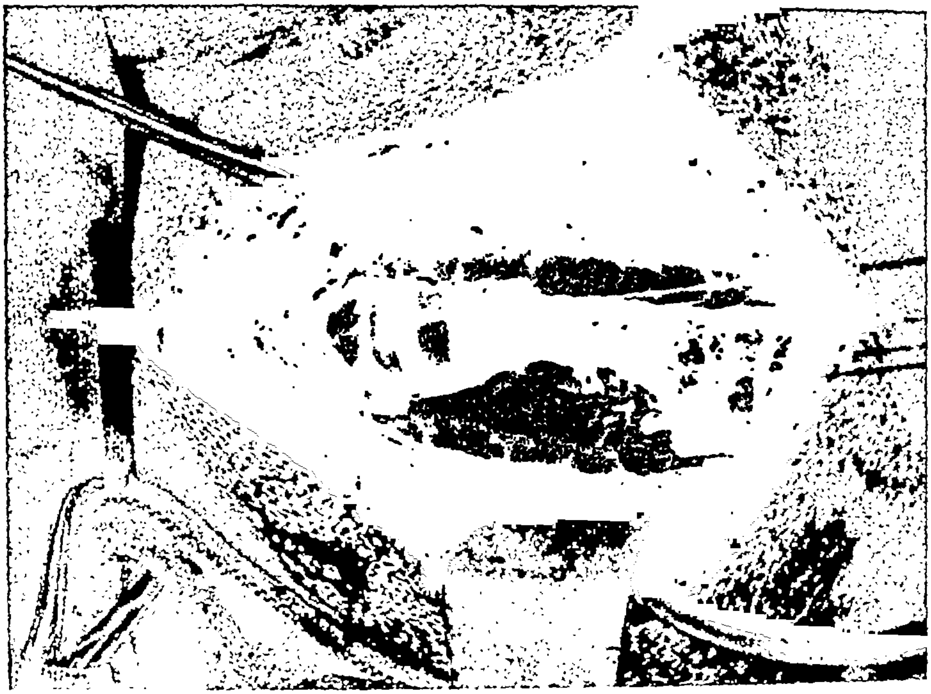

Fig. 4.—Graft in place with "sleeve" type anastomosis as used in Group 2.

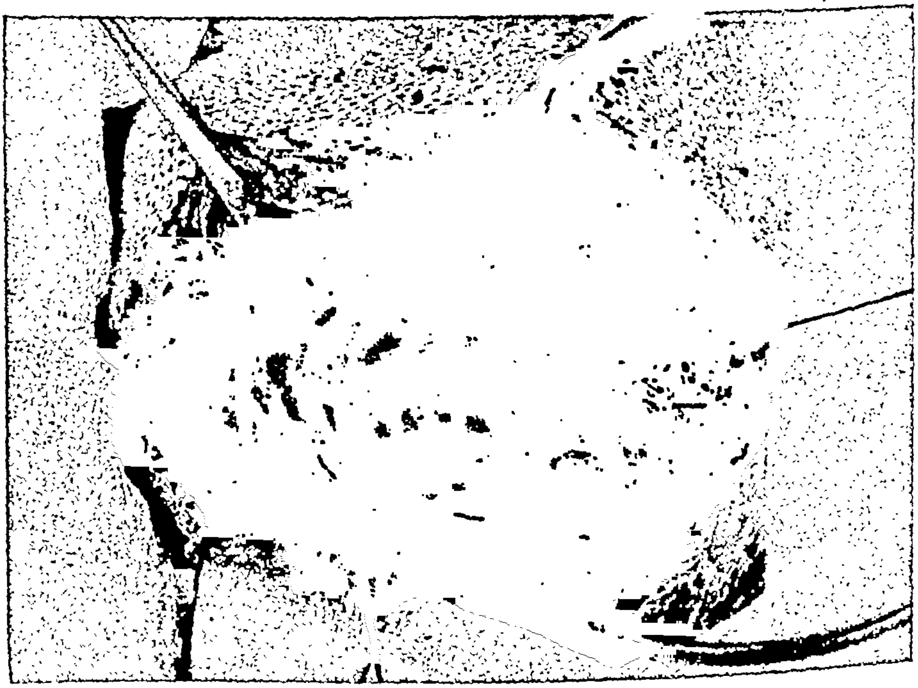

Fig. 5.—Completion of "sleeve" type anastomosis as used in Group 2.

To allow for any disproportion in the size of the trachea, transplants from large tracheas were used in medium- and small-sized animals. Several sizes were always available and not chosen until the host's neck had been opened and the trachea inspected. A selected portion of the trachea was then carefully dissected, care being taken to preserve as much of the peritracheal vascular tissue as possible. The segment to be removed (complete cylinders from one-half to one inch in length) were resected. The transplant was then slipped under both ends of the remaining trachea so that there was an overlap of from one-fourth to one-half inch. The open portion of the transplant was lying in the anterior midline. Both ends were then sutured over the host's trachea using two rows of interrupted 0000 silk at each extremity. The midline of the transplant was then closed with a longitudinal row of interrupted 0000 silk. The strap muscles of the neck were approximated over the area to act as a seal, and also as part of the outer framework of the newly formed trachea itself. Fig. 5 shows the appearance of this type of anastomosis at completion. This procedure circumvented to some extent the mechanical difficulty of sagging in of grafts up to one inch in length and became established as the method of choice in this type of transplantation in the trachea.

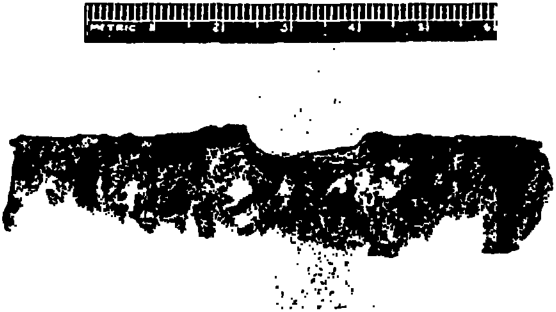

Fig. 6.—Window defect created five months before and closed with preserved transplant. Note loss of symmetry and absence of rings over the grafted area.

Group 1.—In this group five dogs were used.

Square windows were cut from the cartilagenous portion of the trachea measuring approximately one-half of the circumference, the size depending on the size of the trachea. A preserved transplant was put in place using simple end-to-end anastomosis. The postoperative course was uneventful. The dogs were not given penicillin. The only symptoms present were a mild cough and some loss of appetite. They started eating regularly in several days, and the cough disappeared in the second and third weeks. All dogs survived and were sacrificed at periods varying from three weeks to ten months. In two of the dogs transplants were used in the left main bronchus as well as the trachea.

At three weeks the transplant was soft and semirigid. It was thickened and edematous and densely adherent to the neck muscles and surrounding tissues. Microscopic study revealed respiratory epithelium growing in from the edges and covering at least one-half of the graft. Within six weeks it was completely covered. At three weeks there was marked edema of the submucosa.

There was an early ingrowth of fibroblasts which were arranged in linear fashion. The cartilage in the transplants stained pink and retained little of its normal bluish color. A layer of granulation tissue was present on the inner surface of the graft and there was a dense infiltration of lymphocytes of the small round type.

Present also were a smaller number of polymorphonuclear leucocytes. At three months there was considerable thinning of the wall of the graft. The neck muscles were directly adherent to this area preventing to a great extent collapsing of the segment into the tracheal lumen. This was held to be purely a mechanical advantage. *The muscle formed a firm wall on which the transplant* lay, held taut by the tracheal edges. At five months it was impossible to identify the site of anastomosis from the mucosal surface. This could be readily identified from the outer surface however, due to the loss of symmetry and the absence of cartilage rings. Fig. 6 presents such a specimen. One can readily identify the site and extent of the grafted area.

Sections revealed the wall to be very highly vascular during the first three months, but then gradually to thin out and form dense scar tissue. In two specimens there were small areas of calcification in the graft.

All of the animals in this experiment responded well to the grafts. There was no mortality nor was there enough stenosis of the airway to incapacitate the dogs. There was loss of tracheal symmetry at the graft site but this was not a serious effect. One could say that small window defects were successfully closed with preserved tracheal grafts, in animals in which up to one-half of the wall was removed (cartilagenous portion). This was true of bronchial as well as tracheal specimens.

Group 2.—Thirteen animals were used in this series.

All anastomoses were performed as described in Fig. 4. In five consecutive animals one-inch sections were removed and tracheal continuity restored with preserved transplants. All dogs survived and were sacrificed at intervals varying from three weeks to ten months. Gross and microscopic observations were similar to those in Group 1. At three weeks there was growth of respiratory epithelium from the tracheal edges toward the center of the graft. The most central epithelial growth was low columnar in type without cilia. The epithelium near the anastomotic site was mature and ciliated. At six weeks the graft was almost completely epithelialized, and at three months covering with mature ciliated respiratory epithelium was complete. Fig. 7 is a section through the wall showing this epithelium, scar tissue in the wall and absence of cartilage.

The presence of submucosal edema during the first six weeks was constant. Between the columns of ingrowing epithelium, there was granulation tissue. The tissue was markedly edematous, containing a large number of segmented leucocytes but also a high percentage of small lymphocytes. The cartilage was rapidly disappearing at six weeks and at three months, as seen in Fig. 7, was entirely replaced by scar. The wall at this interval was thick and good tracheal continuity was maintained though there was some tendency to sag inward.

At six months, as seen in Fig. 8, the wall of the trachea in the area of the transplant was much thinner than at three months. There was complete absence of cartilage and the scar tissue in the wall was less thick. The neck muscles were dissected from the specimen before photographing but it is felt that this musculature played an important role up to this interval in maintaining the integrity and patency of the tracheal wall in the area of the transplants.

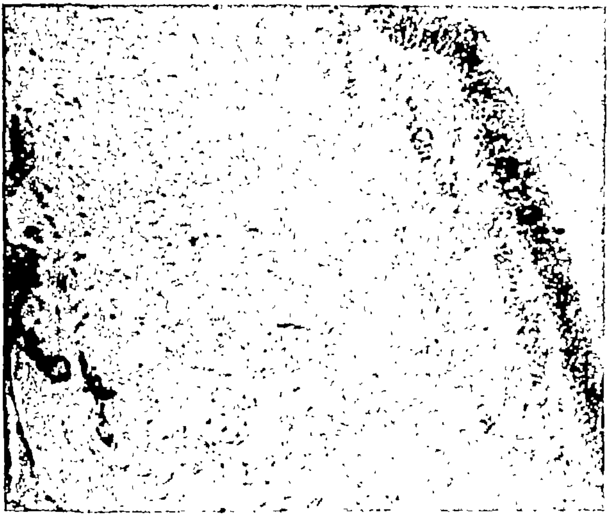

Fig. 7.—Section under high magnification. Graft three months old. Mature respiratory epithelium, dense scar in the wall with absence of muscle and cartilage.

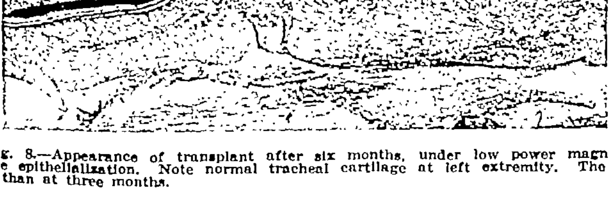

Fig. 8.—Appearance of transplant after six months, under low power magnification. Complete epithelialization. Note normal tracheal cartilage at left extremity. The wall is thinner than at three months.

At six months there was a definite tendency to sagging inwards of the grafted area with a loss of from one-fourth to one-third of the lumen of the trachea. This was undoubtedly due to retraction of the scar tissue and gradual thinning of the tracheal wall.

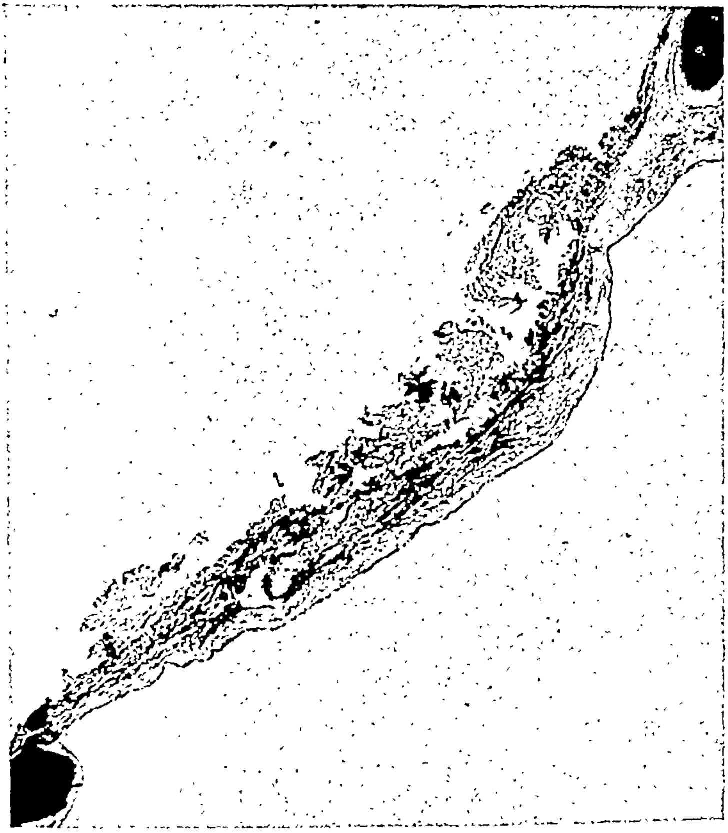

Fig. 9.—Marked thinning of the wall of the transplant. This is after ten months in the host. Neck muscles have been dissected from the wall. Cartilage seen is from the trachea of the host.

Fig. 10.—Gross specimen of the section seen in Fig. 9. The extent of the graft is readily identifiable. This is ten months after transplantation.

At ten months the wall was thinner and there was further loss of tracheal lumen, extending from one-third to one-half of the circumference. Fig. 9 presents a section of the wall at this interval. At either extremity one can see normal tracheal rings which are not a part of the transplant. There is no cartilage present in the graft. Fig. 10 presents the gross appearance of this trachea. The extent of the transplant is easily identified. The dog was not incapacitated in his usual activities around the pen but his activities were restricted by the pen.

In three dogs one and one-half inch segments were removed and transplants put in place. Two of these died during the third week, of strangulation while eating. They were coughing and had been ill since the first week, loosing weight steadily. They were noted to have difficulty in breathing. Both strangled while eating during the third week. Autopsy revealed the trachea in the transplanted area to be extremely soft, pliable, and easily compressed. There was marked sagging inward of the wall reducing the lumen to less than one-half of its normal size. It was felt that the esophagus, filled with a bolus of food, had closed off the trachea completely. The remaining dog was sacrificed at ten months. The microscopic findings were similar to those previously described. However there was a significant loss of tracheal lumen, it being only one-half its normal size. The wall was thin, tough, and fibrous. No cartilage was present, it was easily compressed and it seemed that but for the effect of the neck muscles a fatal obstruction would have occurred early in the postoperative course.

Using four consecutive dogs, two-inch sections were removed and the transplants used to rebridge the defects. All of these dogs coughed severely during the first week, ate very little, and were ill. All four died during the second and third week; three of strangulation while eating and one during the night. Gross examinations revealed a severe sagging inward of the tracheal wall at the transplant site. This portion was a soft, flaccid tube. It was felt that the sagging was of a mechanical nature much the same as a clothesline which, though suspended at either end sags in the middle.

DISCUSSION

The achievement strived for in these experiments was to bridge extensive defects in the trachea, or tracheobronchial segment. It was hoped that long lengths could be resected and continuity be re-established using homogenous tracheal transplants. Our experiments have failed to produce these results. An experimentally successful transplanting should satisfy the following criteria to be deemed worth while.

1. The transplant should become an integral part of the system anatomically.
2. It must satisfactorily meet the functional requirements.
3. A minimum of morbidity should accompany its use.
4. It should present a permanent replacement.

It was wished by us, to accomplish this without the use of foreign materials that might require removal later.

Our failure to meet the preceding criteria is obvious from study of the experiments. Small window defects were successfully closed using these transplants. However, such defects have been covered by others using fascia, plastics, and Gelfoam. The producing of a framework for the ingrowth of tissue was the important factor in these repairs. The repaired portion was not rigid and there was loss of tracheal symmetry. When the defect was not extensive or did not involve over one-half of the cartilaginous portion of the trachea, there was not sufficient loss of luminal circumference to encroach on function. The transplants were covered inside by the ingrowth of epithelium from the ends of the trachea. The cartilage and fibrous tissue within the walls of the grafts slowly underwent liquefaction, absorption, and replacement by scar tissue.

In the experimental animal temporary success was attained in the closure of short complete tracheal defects in lengths not greater than one inch. Histologically and anatomically the same succession of events, as described in the small window defects, were found. Edema, liquefaction, absorption, and subsequent replacement by scar was the succession. Respiratory epithelium readily grew in over the graft from both ends of the trachea and within three months the graft was completely covered. At six weeks there was marked degeneration of cartilage in the graft; at three months there was fibrosis where the cartilage had been. In none of the specimens was there any evidence of regeneration of cartilage within the wall, or of growth from the trachea into the transplant.

As the cartilage disappeared, the transplant became a nonrigid tube lined with respiratory epithelium whose patency was maintained by the suspension effect of the rigid ends of the trachea, and the neck musculature. These muscles were markedly adherent to the wall and actually formed an integral part of it. When they were dissected away from the transplant, the wall partially collapsed. At six months there was a loss of from one-fourth to one-third of the tracheal lumen; at ten months from one-third to one-half was lost. The scar tissue though thick in the first months, thinned out markedly at six and ten months.

When the defect was increased to one and one-half inches in three dogs, two died within three weeks of tracheal obstruction. When this was increased to two inches in four dogs, all died within three weeks. The most common finding was strangulation while eating, though two died during the night. Study of the specimens revealed a soft, edematous, flaccid tube, without support. That fatal obstruction did not occur in the cases where shorter segments were removed was thought to be due to the suspension effect of the divided ends of the animal's trachea and the stabilizing effect of the neck musculature. In other words where longer transplants were used, the resulting flaccid tube was too long for these factors to support and complete early obstruction was inevitable.

In summary it can be said that by the methods used in these experiments, short segments can be transplanted and a soft fibrous tube lined with epithelium up to one inch in length can be produced. However, there follows a gradual narrowing of this segment that will finally lead to obstruction.

It becomes necessary to provide a rigid framework for the formed tubes to prevent their gradual collapse. If this can be done, then the use of homogenous preserved transplants may possibly be successful. Further experimental work on this subject is at present being carried out by us using various materials.

Our experience indicates that a preserved homogenous graft is superior to a fresh one. This seems true due to the milder tissue reaction in the host and less tendency to massive liquefaction. There is a retarding of these processes with the use of preserved, nonviable, homogenous transplants.

CONCLUSIONS

1. Experiments have been reported in detail using homogenous tracheal transplants in the repair of tracheal defects.

2. The end results have been a failure in the repair of extensive defects due to the absorption and nonreplacement of cartilage, leaving a flaccid fibrous tube that eventually collapsed sufficiently to cause tracheal obstruction. Some temporary success was obtained in repair of short defects due to the suspension effect of the ends of the animal's trachea and the neck musculature.

3. There was no evidence of generation or regeneration of cartilage in or into the transplanted segment.

4. A method of preservation of transplants is described.

5. The use of preserved tracheal transplants is preferred to those in the fresh state.

6. A technique for securing the transplants in place which is felt to be preferable to simple end-to-end anastomosis is described in detail.

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(See discussion on page 647.)

RESECTION OF THE TRACHEA AND BRONCHI

An Experimental Study

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THORACIC surgeons have been plagued by the technical problems concerned with the surgical treatment of tumors and strictures involving the trachea and major bronchi. There have been two principal obstacles to resection; first, the maintenance of an adequate airway during the operative procedure and second, the reconstruction of the segment so that it may resume normal physiologic function.

Malignant tumors extending into the carina, adenomas extending from a purely lobar origin into a main-stem bronchus, and various types of bronchostenosis constitute commonly encountered situations where reconstructive procedures could conceivably restore function without undue sacrifice of pulmonary tissue. A review of these problems and a survey of the experimental efforts of others, have suggested criteria which must be satisfied if physiologically adequate tracheal or bronchial reconstructions are to be performed.

These criteria demand (1) that an adequate airway must be maintained to the lungs during the procedure with, at most, only a brief interruption of intrabronchial closed circuit anesthesia, (2) that an airtight reconstruction of the defect must be obtained, (3) that rigidity must be sufficient to avoid postoperative respiratory "flutter" at the site of repair, (4) that the reconstruction must facilitate a mucus-free postoperative period, (5) that healing must be complete without late stenosis, and (6) that there must be minimal bacterial contamination at operation.

HISTORICAL REVIEW

Taffel demonstrated in 1940 that small tracheal defects could be closed successfully with patches of fascia lata. The grafts, applied with interrupted silk sutures which did not penetrate the lumen of the trachea, did not remain viable but acted as a scaffold for invading fibroblasts.[1] Daniel, repeating these experiments, found that stenosis occurred in the grafted areas. Later, glass and stainless steel tubes were inserted into tracheal defects and regeneration of tissues occurred around these including new growth of cartilage as well as mucosa.[2] Grindlay, Clagett, and Moersch have used polyethylene tubing for experimental reconstruction of the trachea.[3] No cartilage was found in the regrown tracheal wall of five dogs examined one and one-half to eleven months postoperatively,

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but apparently little stenosis developed in most and retention of secretions was not a problem.[4] Clagett, Grindlay, and Moersch reported the use of polyethylene tubing in one human case without success.[5]

Hanlon reported the successful use of gelatin sponge for the closure of small experimentally produced defects in the bronchi of dogs.[6] Gough used alginate gels (seaweed preparations) for closing similar small defects during the surgical treatment of pulmonary tuberculosis in human beings.[7] End-to-end anastomosis of divided bronchi, both with and without excision of experimentally produced strictures, has been reported by Jackson and associates. They developed an everted cuff method of closure that appears satisfactory.[8]

However, in spite of advances toward a solution of the problem, no one of these methods fulfills all the criteria for a physiologically adequate tracheobronchial reconstruction. With these criteria in mind, we have conducted further animal experiments which have resulted in one solution of certain aspects of the problem.

METHOD AND MATERIAL

Eighteen mongrel dogs were used in this study and more than one operation was performed on some animals. Anesthesia was achieved with 6 per cent Nembutal solution intravenously and aseptic operating room technique was always observed. All operations were performed transpleurally using interrupted positive pressure oxygen insufflation through a simple endotracheal tube made airtight by gauze packing in the throat of the anesthetized animal.

Four types of experiments were performed. In the first series of four experiments, the airway was divided and reunited by interrupted silk sutures through all the layers around adjacent cartilage rings. Two of these animals survived a significant period, one for eight months and one for four and one-half months. Of those not surviving, one failed to recover from the anesthesia, and in the other the anastomosis of the trachea was insecure resulting in bilateral tension pneumothorax (Table I).

A Foley catheter was used as an airway in the first set of experiments. The balloon end was introduced as far as the carina so that the trachea could be manipulated at a point proximal to the balloon. This same method was used in the second set of three experiments wherein whole segments of the trachea were excised and the defects reconstructed with tantalum gauze lined by pleura or fascia. These experiments were technically difficult, air leaks were frequent, and the longest survival time of an animal was only seven days (Table II).

From the first series of experiments it became apparent that simple through-and-through sutures about adjacent cartilage rings were satisfactory and that an inlying tracheal tube placed prior to operation in the manner of a bronchospirometric catheter would permit manipulations with the trachea open. However, the problem of excision in the region of the carina, where many of the resectable pathologic lesions exist, together with a satisfactory method of plastic repair, remained to be solved.

An inlying tube, placed in the tracheal lumen through the operative wound, had been used in the last of the tantalum experiments with success. This tube was therefore used in the third set of ten experiments in which either pneumonectomy or lobectomy was performed. The resected bronchus was divided flush with its parent stem, sometimes removing a portion of the parent stem as well. The remaining aperture was then closed by applying a patch from the wall of a small bronchus in the resected lobe or lung. Patches were first applied to the outside of the defect and secured with interrupted sutures. Air leaks were frequent by this method. Later the grafts were tailored, placed inside the lumen of the affected bronchus, and secured with two interrupted sutures for closure with a continuous suture of fine silk. In this group of ten experiments there were four survivors, sacrificed at intervals from thirty-four days to nine months postoperatively (Table III).

TABLE I. DATA FROM FOUR EXPERIMENTS OF BRONCHIAL OR TRACHEAL DIVISION AND RESUTURE

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	CONDITION OF OPERATIVE SITE	PENICILLIN	SURGICAL AIRWAY
D1 - E1	Right upper lobe bronchus, division and reanastomosis	Interrupted 00 silk	8 months 4 days	Reoperation on trachea	Well healed. No stenosis. Good mucosal lining	+	None
D3 - E2	Division one-half of trachea and resuture	Interrupted 00 silk	3 days	Technical failure of airway. Bilateral pneumothorax		+	Foley catheter
D3 - E3	Complete division of trachea and resuture	Interrupted 00 silk	4½ months	Sacrifice	No stenosis. Mucosa covered stutures	0	Foley catheter
D18 - E19	Removal three tracheal rings and resuture	Interrupted 000 silk	Did not recover from anesthesia			+	Rubber tube

TABLE II. DATA FROM THREE EXPERIMENTS OF TRACHEAL RESECTION AND TANTALUM GAUZE REPAIR

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	PENICILLIN	SURGICAL AIRWAY
D4 - E4	Resection three tracheal rings—tantalum and pleural patch	Interrupted 00 silk	7 days	Pneumonia; obstruction due to narrowed tantalum repair	0	Foley catheter
D5 - E5	Resection two tracheal rings—tantalum and pleural patch	Interrupted 00 silk	1 day	Did not recover from anesthesia	0	Foley catheter
D6 - E6	Resection two tracheal rings—tantalum and fascia patch	Interrupted 00 silk	At operation	Leak and tension pneumothorax	0	Tube

TABLE III. DATA FROM TEN EXPERIMENTS OF LOBECTOMY OR PNEUMONECTOMY AND AUTOGRAFT REPAIR

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	CONDITION OF OPERATIVE SITE	PENICILLIN	SURGICAL AIRWAY
D8 - E8	Right upper lobectomy. Autograft outside	Interrupted 000 silk	2 days	Leak; bilateral pneumothorax		0	Tube
D9 - E9	Left upper lobectomy. Autograft outside	Interrupted 000 silk	9 months	Sacrifice	No stenosis and sutures covered by mucosa	0	Tube
D10 - E10	Left pneumonectomy	Not completed	At operation	Cardiac arrest			Tube
D3 - E11	Left pneumonectomy. Autograft outside	Interrupted 000 silk	45 days	Sacrifice	Graft viable; no stenosis; sutures covered	0	Tube
D11 - E12	Right pneumonectomy. Autograft outside	Interrupted 000 silk	Did not recover from anesthesia. Tension pneumothorax				Tube
D12 - E13	Right upper lobectomy. Autograft inside	Continuous 00000 silk	34 days	Sacrifice	Graft viable; no stenosis; sutures covered	0	Tube
D13 - E14	Right pneumonectomy. Autograft inside	Continuous 00000 silk	At operation	Cardiac arrest			Tube
D14 - E15	Right pneumonectomy. Autograft inside	Continuous 000 silk	Day of operation	Incomplete expansion, left lung		+	Tube
D15 - E16	Left pneumonectomy. Autograft inside	Continuous 000 silk	Day of operation	Incomplete expansion, right lung		0	Tube
D16 - E17	Left pneumonectomy. Autograft inside	Continuous 0000 silk	51 days	Sacrifice	Graft viable; no stenosis (edges not well tailored, however)	0	Tube

TABLE IV. DATA FROM THREE EXPERIMENTS OF TRACHEAL RESECTION AND HOMOGRAFT REPAIR

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	CONDITION OF OPERATIVE SITE	PENICILLIN	SURGICAL AIRWAY
D9 - E20	Resection of four tracheal rings. Insertion of three-ring fresh (two hour) homograft	Interrupted 000 silk plus Gelfoam	7 months 19 days	Sacrifice	Marked stenosis with fibrous replacement of homograft	+	Tube
D1 - E21	Resection of four tracheal rings. Insertion of four-ring homograft. (Iced 21 days at -4° C.)	Interrupted stay sutures. Continuous 000 silk	Died at conclusion of operation	Graft too small in diameter. Tube could not be removed		0	Tube
D20 - E22	Resection of three tracheal rings. Insertion of four-ring homograft. (Iced 51 days at -4° C.)	Interrupted stay sutures. Continuous 000 silk	Living four months postop. but with wheeze		Bronchoscopy at 45 days showed short granulations and suggestive early stenosis at graft site	+	Tube

In the final group of three experiments, resected portions of the trachea were replaced with complete tracheal homografts from donor animals. A fitted tube airway was introduced at operation as before. The grafts were held with four interrupted sutures while a continuous stitch was placed at each end to make an airtight seal. A fresh homograft, two hours old, was inserted in one of these experiments. Homografts, stored at -4° C. for twenty-one and fifty-one days, respectively, were used in the other two. One animal died because the donor tracheal segment was too small and the procedure was therefore technically impossible. Of the two surviving animals, one was sacrificed at seven and one-half months and the other is living and well five months postoperatively (Table IV).

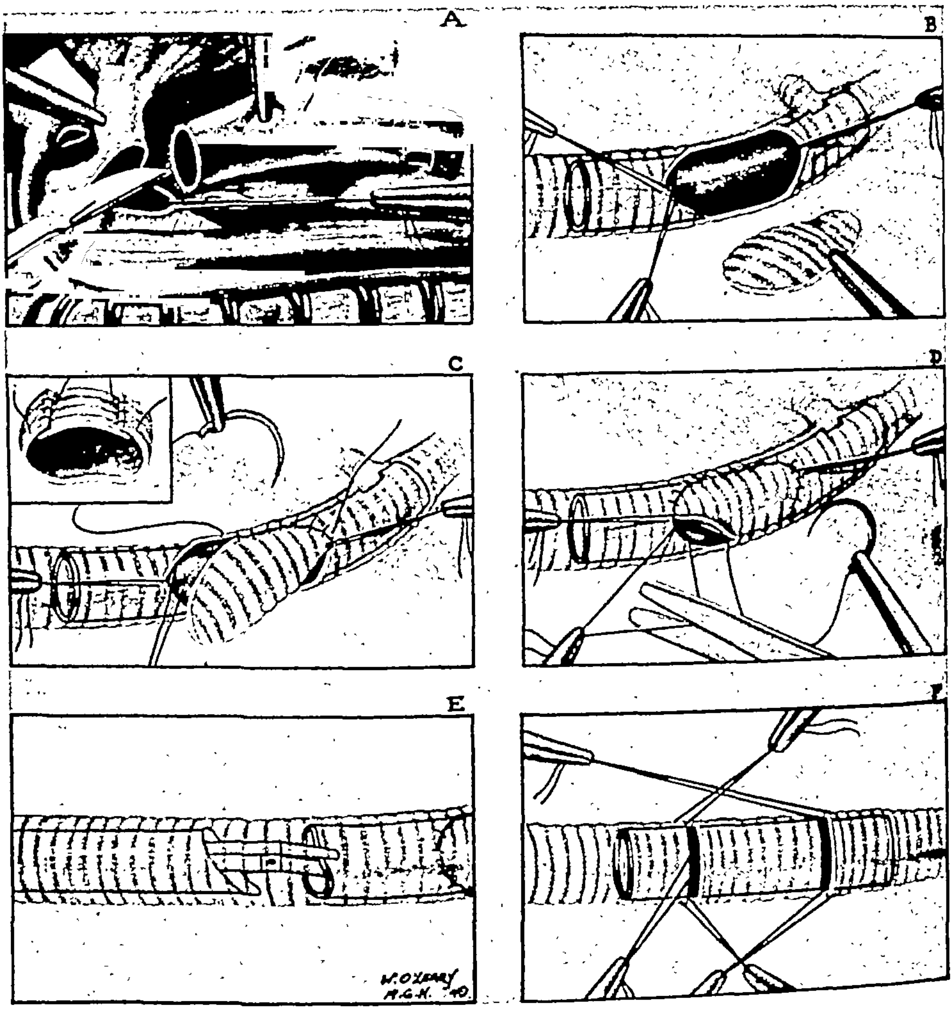

Fig. 1.—Drawing of the technique for insertion of a rubber airway tube and autograft in the radical resection of the right lung (dog). Drawings *A* through *E* illustrate right pneumonectomy as described in the text and *F* illustrates the use of the airway for resection of a complete segment of the trachea and its repair.

TECHNIQUE

For pneumonectomy, an anterolateral incision through the fourth intercostal space was used. A routine resection was performed with individual ligation and division of the hilar structures. The technique for insertion of the airway tube and repair with an autograft following right pneumonectomy is illustrated by the drawings in Fig. 1.

After the bronchus was cleared, an incision was made in the carinal angle sufficient to admit the rubber tube (Fig. 1, *A*). A guide suture of 000 Deknatel silk was placed on the lower lip of the opposite main stem for its elevation during insertion of the rubber airway. A window was cut in the side of the airway near the distal end and a stay suture was looped through the wall of the tube on the side opposite the window. The tube was inserted from below upward until it lay within the tracheal lumen. Traction was then made both on the distal bronchial stay suture and on the tube traction suture so that the tube slipped down into the opposite main-stem bronchus where it lodged with the distal window opposite the left upper lobe orifice (Fig. 1, *B*).

When the division of the main stem was almost complete, a second traction suture was placed on the upper cut end and the resection completed. A graft was then fashioned from the cartilaginous portion of a bronchus in the resected lung. This was fitted with approximately two millimeters of overlap beyond the edges of the defect. A fine French needle was threaded on one end of the lower stay suture and this was used as the first anchoring stitch. A continuous suture of 000 or 0000 Deknatel was then started at the anchoring stitch. The sutures were placed from the inside of the defect outward and the edges of the graft were tucked under the edges of the defect so the graft lay within the tracheal lumen (Fig. 1, *C*). When the suture was complete on one side, an anchoring stitch was made from the second stay suture, and the continuous stitch was tied to this. The remaining circumference of the graft was then attached with a similar continuous suture. When only a small window remained, the traction suture on the tube was cut and removed (Fig. 1, *D*). The final stitches were placed and the reconstruction tested for leaks by covering it with saline while endotracheal positive pressure was made by the anesthetist. Rarely, a leak was found, and closed by a single stitch. A strip of Gelfoam was sometimes placed over the patch. The mediastinal pleura was closed over the site of the graft, the hemithorax irrigated, and the thoracic wound closed in routine fashion.

When the pressure in the hemithorax had been adjusted so that positive pressure anesthesia was no longer necessary, the Jackson bronchoscope was passed, the edge of the inlying rubber tube grasped with an ordinary biopsy forceps, and the tube and bronchoscope withdrawn together (Fig. 1, *E*).

Complete segment homografts were also placed in the trachea by the use of the inlying airway. The tube was inserted through the initial tracheal incision and stay sutures were placed on opposite sides of each cut end to counteract the normal tendency of the trachea to retract. After a segment of donor trachea was prepared, the distal (caudal) end of the tube was removed, the donor segment was slipped over it like a ring, the tube reinserted in the distal trachea and pulled into position by the traction suture. The stay sutures were first passed through the graft to secure it in position and a continuous stitch around adjacent cartilages completed the anastomosis at either end (Fig. 1, *F*).

Several technical points should be reviewed. A variety of tubes of graduated diameters was available for each operation. The tube selected was of a diameter to wedge snugly into the left main stem at the level of the left upper lobe orifice and it was of sufficient length to extend at least one and one-half inches beyond the upper margin of tracheal resection. The tube functioned as an internal tracheal splint by which the entire area could be elevated with traction on the tube suture. Furthermore, the tube then could not slip from the trachea or bronchus during repair, an accident which did occur early in the series. Since the tubes did not taper, slight leakage of air occurred on the tracheal end but this was readily compensated for by the anesthetist. The orifice in the tube opposite the left upper lobe bronchus was necessary to permit aeration of that lobe. The distal traction suture on the left main stem was imperative so that the edge could be elevated when the tube was drawn downward to glide into proper position. The method worked equally well for either lobectomy or pneumonectomy.

RESULTS

All experiments have been summarized in Tables I to IV. Complete healing occurred after division of either the trachea or bronchus and simple resuture with interrupted silk. The sutures were covered by a cellular layer even in that portion which lay within the lumen of the trachea or bronchus and stenosis was never demonstrated (Fig. 2).

After resolution of technical difficulties, the method of autografts was found to work satisfactorily. Gross specimens from the surviving animals, taken after sacrifice, showed no stenosis of grafted areas following either lobectomy or pneumonectomy (Figs. 2 and 3). Microscopic examination of the grafts revealed firm healing with a minimum of inflammation, almost no fibrosis, and even viable cartilage in the transposed segments (Figs. 4 and 5). If the graft was poorly fitted outside the tracheal lumen, some granulations occurred with metaplasia of epithelium over these zones of malposition. In well-fitted grafts however, the epithelium retained its columnar and ciliated character even at the line of junction with the normal bronchus (Fig. 6). One badly fitted graft, with overlap on the interior of the trachea, nevertheless remained viable and

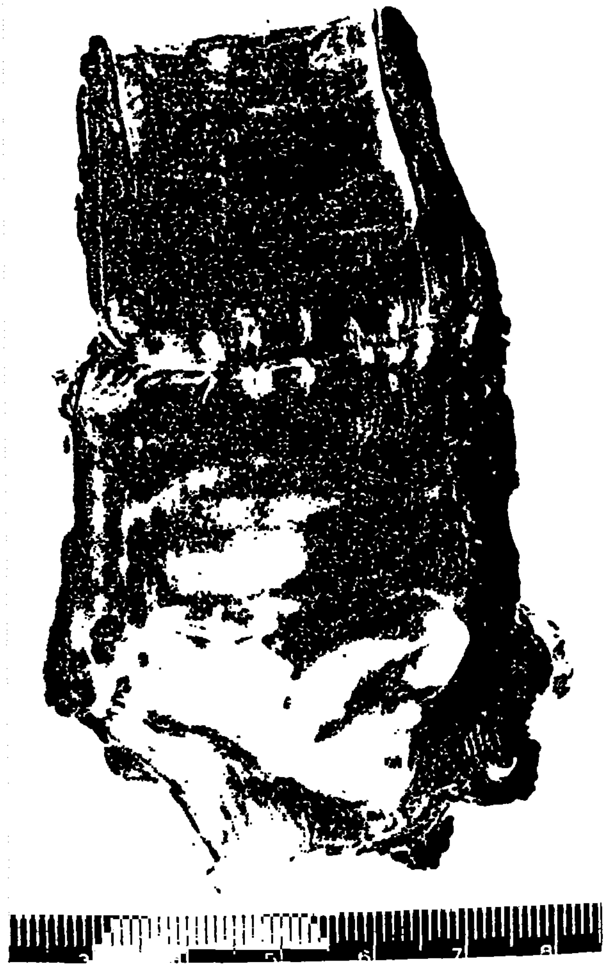

Fig. 2.—Photograph of gross tracheal specimen from Dog 3; simple division and resuture of the trachea four and one-half months previously. Note firm healing without stenosis and cellular layer covering silk sutures (Experiment 3). A left pneumonectomy with autograft had been performed forty-five days prior to sacrifice. Note complete healing without stenosis (Experiment 11).

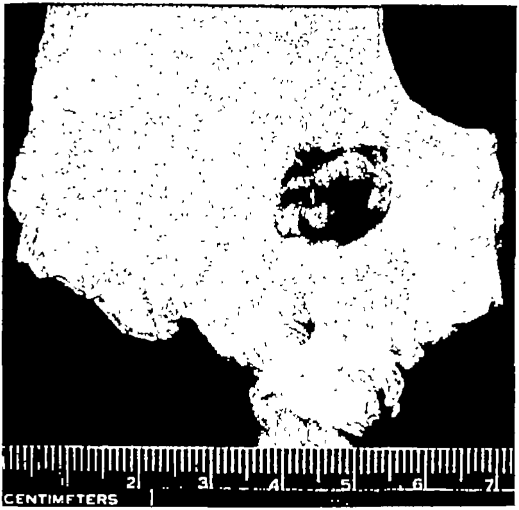

Fig. 3.—Photograph of gross specimen showing a poorly fitted autograft thirty-four days following a right upper lobectomy. The graft was viable but of unusual color since four hours elapsed from death to time of photograph (Experiment 13).

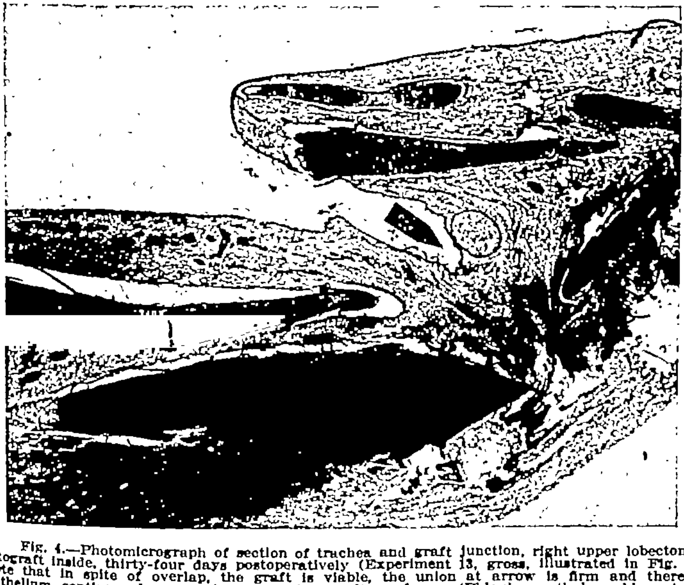

Fig. 4.—Photomicrograph of section of trachea and graft junction, right upper lobectomy, autograft inside, thirty-four days postoperatively (Experiment 13, gross, illustrated in Fig. 3). Note that in spite of overlap, the graft is viable, the union at arrow is firm and there is epithelium continuously over the upper (mucosal) surface. (Phloxine-methylene blue stain, ×40.)

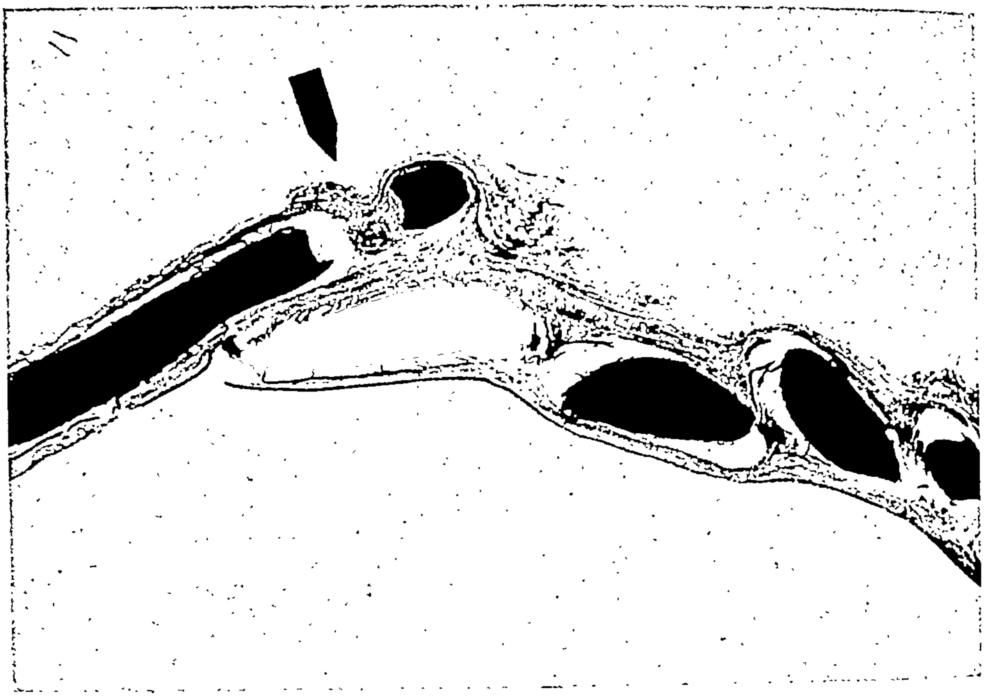

Fig. 5.—Photomicrograph of section of autograft placed inside lumen following left pneumonectomy fifty-one days previously (Experiment 17). Note integrity of entire graft, intact mucosa, except at junction where microtome caused artifact, and the simple resorption of a portion of tracheal cartilage where pierced by a silk suture, shown at arrow. (Phloxine-methylene blue stain, ×18.)

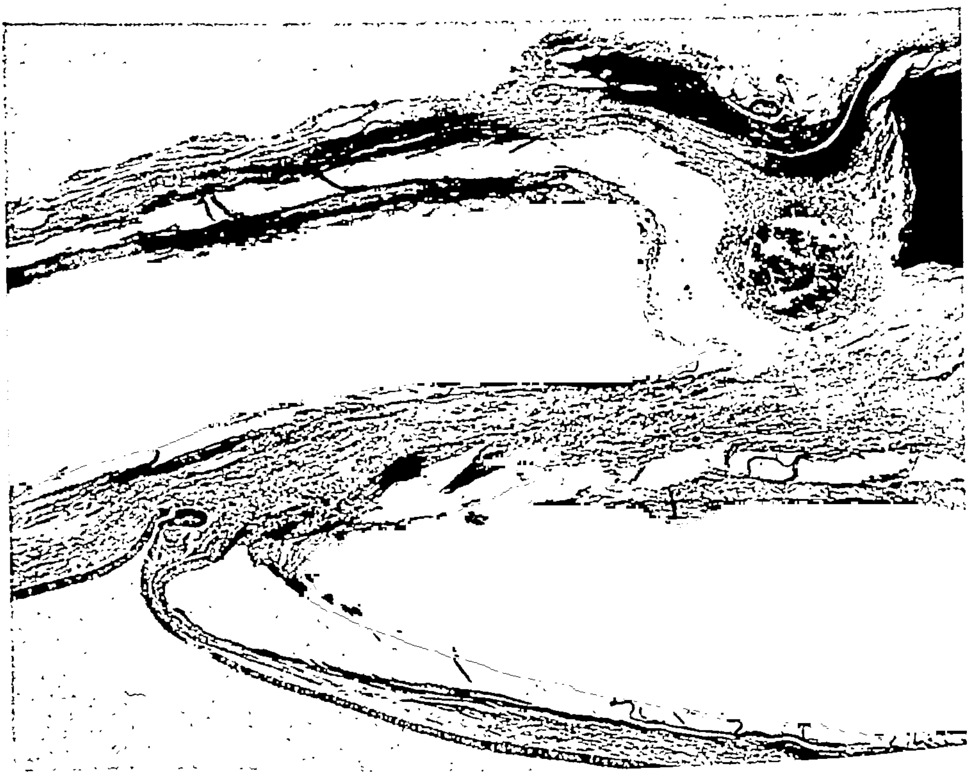

Fig. 6.—Photomicrograph at higher power of junction of autograft (below) with trachea (above), already shown in Fig. 6 (Experiment 17). Note firm healing, minimal inflammation, and the unusually normal ciliated columnar epithelium, even at the line of union. (Phloxine-methylene blue, ×50.)

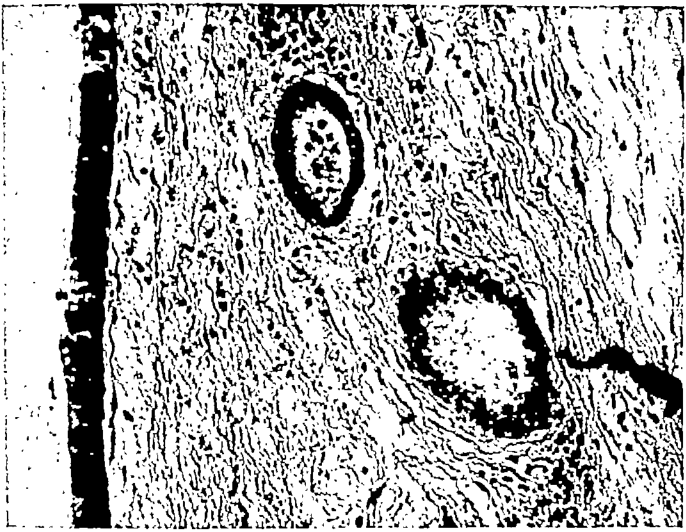

Fig. 7.—Photomicrograph of center of autograft already shown in Figs. 3 and 4 (Experiment 13). Note viable normal epithelium and bronchial glands. A few mononucleated cells of chronic inflammation are present. (Phloxine-methylene blue, ×400.)

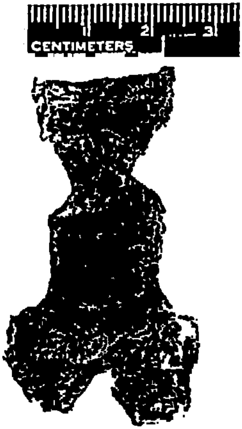

Fig. 8.—Photograph of gross specimen from Dog 9 showing marked stenosis of trachea at site of tracheal homograft seven and one-half months previously (Experiment 20). Intact left main-stem bronchus with autograft following left upper lobectomy nine months previously is seen at the lower right. Note lack of stenosis (Experiment 9).

its edges were covered by a proliferating pseudosquamous epithelium (Fig. 4), while in its central portions, the normal ciliated epithelium remained and even bronchial glands were retained (Fig. 7).

Of the two animals surviving homografts, only one was sacrificed. Prior to sacrifice the animal developed a marked wheeze and at autopsy there was pronounced tracheal stenosis caused by resorption of the homograft and replacement with fibrous and granulation tissue. The internal diameter of the lumen in the center of the graft was reduced to 0.5 cm. from a normal of 1.8 cm. in an interval of seven and one-half months (Fig. 8). Microscopically, death of the graft was evident with proliferation of granulation tissue, acute inflammation and metaplasia of the mucosa where it attempted to grow from the normal tissue to the graft (Fig. 9).

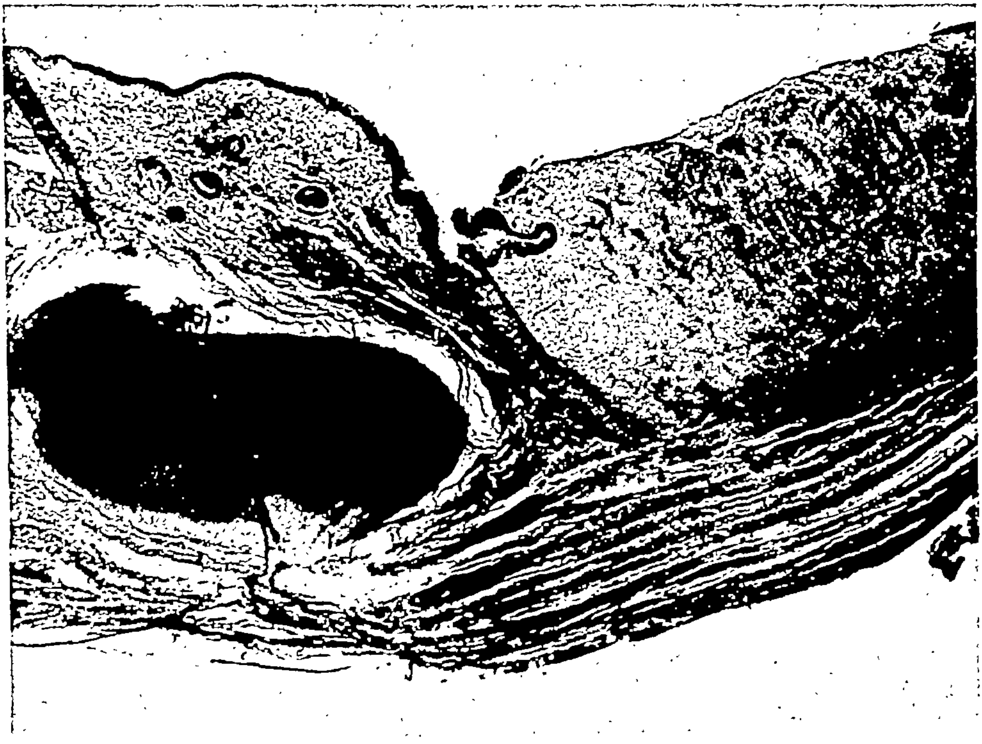

Fig. 9.—Photomicrograph of section of homograft shown in Fig. 8. Note replacement of graft by granulation tissue with fibrous proliferation on its external surface, seen at bottom of picture. Mucosal proliferation with marked metaplasia is present at the junction of normal trachea with replaced graft. (Phloxine-methylene blue. ×40.)

Bronchoscopy of the remaining homograft animal showed granulation tissue and slight stenosis occurring two months postoperatively although the dog was clinically well.*

In all experiments where an airway was placed in the trachea through the operative field, the tube was easily removed postoperatively with the bronchoscope.

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*A respiratory wheeze was apparent in this animal four months after operation. This dog was used for a cardiac experiment performed by another investigator and the tracheal graft segment unfortunately was not saved. A portion of the trachea distal to the graft was preserved and this was normal.

The experiments with tantalum gauze failed because it was almost impossible to secure an airtight closure. However, they did confirm the impression gained in the first series of experiments, that a tube correctly placed would permit maneuvers to be performed on the opened trachea without undue haste.

Infection was not present in the pleural space of any animal although intrathoracic penicillin was used in only six of the twenty experiments. Antibiotics were not used by any other route. Bacteriologic cultures of small bits of tissue from the graft segments taken both before and after preservation by cold showed no growth.

Interruption of bronchial vessels and nerves incident to the complete dissection of bronchi or the trachea apparently did not adversely affect the healing process.

DISCUSSION

The radical resection of the lesions involving the carina or the opposite main-stem bronchus by insertion of glass and plastic tubes has heretofore been only partially successful. This maneuver must be done with great rapidity because of the serious consequences following anoxia of even very brief duration.[9] The method here described, using rubber tubes inserted through a small incision at the beginning of bronchial resection, offers a certain way of maintaining the flow of gases under positive pressure to the remaining pulmonary tissue while permitting careful dissection of the lesion. Further, the inlying airway acts as a prosthesis around which the bronchus or trachea may be more easily reconstructed. Postoperative removal of the tube eliminates the necessity for a permanent inlying foreign body.

Relatively large defects in a bronchus or trachea can be repaired by autografts in those cases in which pulmonary resection is performed. The objection raised at once is that the segment of resected lung might contain tumor or abscess so that either neoplastic disease or infection would prevent the use of smaller bronchi as grafts. This undoubtedly would be true occasionally. However, since the diameter of a tube is small compared to its circumference, grafts of a size adequate to repair a flush bronchial resection may be fashioned from bronchi of relatively high order, hence at a considerable distance from the primary lesion.

We suggest that a method is now available for bronchial reconstruction that is applicable to most situations requiring partial bronchial or carinal resection and which satisfies all of our originally established criteria. The insertion of a tube, removable at the conclusion of the operation, works equally well on either a lobar or main-stem bronchus and maintains a patent airway to the functioning pulmonary tissue with minimal leakage of air during the operation. An autograft, tailored and applied inside the lumen with a continuous suture, makes an airtight closure, has the firmness of normal trachea or bronchus without abnormal rigidity, offers the same mucosa-covered surface as normal bronchus for the retention of mucus during tussive effort, and heals firmly without fibrous stenosis. The preoperative preparation of an assortment of varying sized tubes which are introduced through the sterile operative wound rather than through the mouth of the patient and the proper selection of an autograft from resected tissue provide a technique by which bacterial contamination may be kept at a minimum.

Possible clinical applications for this technique are at once apparent. A relatively benign tumor, such as bronchial adenoma, is occasionally found in such a situation that resection of the lung is necessary because of encroachment on the main-stem bronchus. This might be converted to a lobectomy with salvage of the main stem and remaining lobe or lobes. Occasionally a carcinoma is found growing from the main stem into the carina which is sufficiently localized that pneumonectomy would be feasible if a method of plastic repair were available for a hemisected opposite main stem. This method could not be interpreted as changing the ultimate cure rate of such lesions but, since these tumors usually obstruct completely and cause asphyxia or suppuration distal to the carina, worth-while palliation might be achieved. It should be possible in such cases to obtain a small area of bronchus free from tumor and without severe bacterial invasion in its walls, which could be adequately cleansed with saline to permit its use as a graft.

Benign strictures of a lobar or main-stem bronchus might be excised and end-to-end suture achieved by the use of an inlying tube. Indeed, Griffith ingeniously resected a simple stricture of the left main stem without such help,[10] and Tuttle anastomosed a left upper lobe bronchus directly to the left main stem following radical incision in a difficult lower lobectomy.[11] Gebauer reported the use of dermal grafts in the reconstruction of tuberculous bronchostenosis.[12] However, in a patient with borderline pulmonary function, the tube method might make repair possible when even temporary interruption of airflow to a lobe or lung would exclude surgery entirely. Finally, for those accidents of surgery when more extensive incision is made than intended, the method described might permit the surgeon to recoup his position without undue risk to the patient or loss of functioning pulmonary tissue.

Lesions of the trachea requiring complete excision of several rings are probably still best treated by previously described methods, notably that of Grindlay and his colleagues. Belsey reported an ingeniously handled case where all but a narrow strip of trachea was resected for an adenoma and repair effected with fascia lata over a framework of stainless steel wire.[13] No late follow-up is available. Recently, Rob and Bateman have successfully repaired a defect in the cervical trachea with tantalum gauze and fascia lata.[14] We hoped, rather skeptically, that homografts would remain viable. Although this is not so, they do offer an excellent method of immediate repair and function well for about four months. They are, of course, not clinically applicable at the present time. It is conceivable that a small tracheal lesion, involving no more than three or four cartilage rings, could be resected and end-to-end suture be performed over a tube. This has already been performed experimentally over plastic tubes which are allowed to remain in the trachea.[3]

The ease with which sections of trachea may be removed and the airway maintained with a tube placed at operation, demonstrates the usefulness of the method for testing other types of plastic repair. It is hoped that some adaptation, possibly involving autografts with bronchus from a deliberately sacrificed lobe, will make resection of the isolated tracheal lesion an acceptable technical maneuver.

SUMMARY

A series of animal experiments have been performed to develop a method of radical bronchial resection and repair. Autografts with segments of bronchus from the resected lobe or lung, have been found to possess the correct characteristics for a satisfactory postoperative recovery in addition to remaining viable for complete healing without the development of fibrous stenosis.

The use of a rubber tube for the maintenance of an airway to the remaining lung at operation is described together with the technique of autograft repair.

Homografts of complete tracheal segments from donor animals, inserted by a similar technique, have been shown to function well through the immediate postoperative period but result in gradual resorption and the late development of fibrous stenosis at the site of repair.

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(See discussion on page 647.)

FURTHER EXPERIENCES WITH DERMAL GRAFTS FOR HEALED TUBERCULOUS STENOSIS OF THE BRONCHI AND TRACHEA

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WIRE-ENFORCED, dermal grafts have been used in eleven patients for the correction of severe, healed, tuberculous bronchostenosis or tracheal stenosis. The first four patients have been reported in detail.[1] Of the remaining seven patients, two had dermal grafts inserted in the trachea. In the first of these (Case 7), a separate, severe stenosis of the right bronchus was treated with a second dermal graft at the time of the tracheal operation. This patient has been reported.[2] The second patient had a right pneumonectomy, in addition to the tracheal graft, and died three days after operation. If pneumonectomy had been avoided, as in the first case, the result might have been favorable. Both of these patients have been reported in detail, with two other instances of severe, tracheal stenosis, to emphasize the differences in anesthesia and operative procedure, between bronchial and tracheal surgery.[3]

This paper is based on the whole experience. Its main object is to demonstrate the usefulness of wire-enforced dermal grafts, and to guide other surgeons in their application. Only those cases heretofore unreported are summarized, and the operative technique is not repeated.

Chart I supports the generally accepted fact that usually excisional surgery is required in severe, tuberculous bronchostenosis, but that successful collapse occasionally can be practiced. Also, it discloses a significant number of patients in whom a direct surgical attack on the bronchial lesion itself is indicated, thus permitting a salvage of lobes or lungs free of disease or healed.

Of 136 patients with definite tuberculous tracheobronchitis, 46 per cent came to surgical treatment. Undoubtedly some of the 20 per cent still under medical treatment will require future surgery. The chart possibly assigns a false importance to modern surgical treatment, for many of the surgical patients developed stenosis before the days of streptomycin. A limited experience to date indicates that future use of this substance and PAS will reduce the incidence of bronchostenosis, decrease its mortality, and the percentage of patients requiring surgery, and simultaneously increase the number healed by medical treatment alone. Conversely, the use of these items might enable patients to survive extensive disease, of a type ordinarily fatal without their use, and thereby increase the number requiring surgery and direct treatment of stenotic, tracheobronchial lesions. Nevertheless, it is felt that the administration of streptomycin and PAS, and other drugs likely to be forthcoming, will make tracheobronchial surgery unnecessary more times than it will cure patients to a point where surgery can be done. At this time, it is

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fitting to state that without streptomycin, PAS, or both, dermal grafts for tracheobronchial lesions probably would have a low incidence of success as far as tuberculosis is concerned. Therefore, it is believed that, whereas a definite field for dermal grafts and tracheobronchial surgery in the treatment of tuberculosis exists at the present time, it is likely to diminish because of present and future trends in medical treatment.

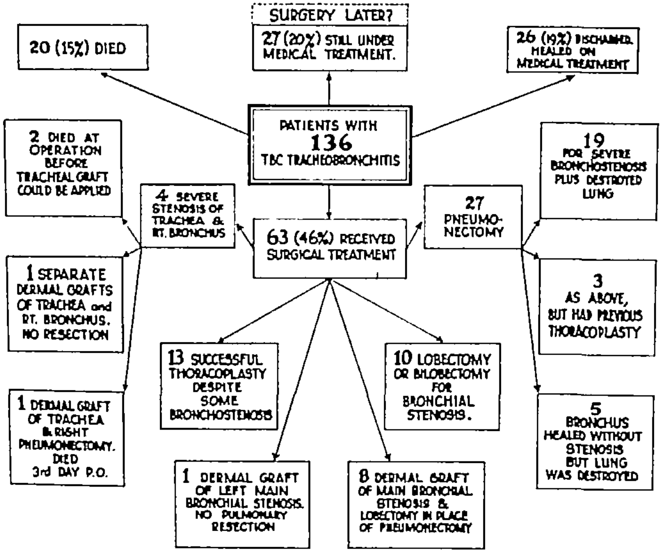
SURGERY LATER?
27 (20%) STILL UNDER MEDICAL TREATMENT.
20 (15%) DIED
26 (19%) DISCHARGED HEALED ON MEDICAL TREATMENT
PATIENTS WITH 136 TBC TRACHEOBRONCHITIS
2 DIED AT OPERATION BEFORE TRACHEAL GRAFT COULD BE APPLIED
4 SEVERE STENOSIS OF TRACHEA & RT. BRONCHUS
63 (46%) RECEIVED SURGICAL TREATMENT
27 PNEUMONECTOMY
19 FOR SEVERE BRONCHOSTENOSIS PLUS DESTROYED LUNG
1 SEPARATE DERMAL GRAFTS OF TRACHEA and RT. BRONCHUS. NO RESECTION
3 AS ABOVE, BUT HAD PREVIOUS THORACOPLASTY
13 SUCCESSFUL THORACOPLASTY DESPITE SOME BRONCHOSTENOSIS
10 LOBECTOMY OR BILOBECTOMY FOR BRONCHIAL STENOSIS.
1 DERMAL GRAFT OF TRACHEA & RIGHT PNEUMONECTOMY. DIED 3rd DAY P.O.
5 BRONCHUS HEALED WITHOUT STENOSIS BUT LUNG WAS DESTROYED
1 DERMAL GRAFT OF LEFT MAIN BRONCHIAL STENOSIS. NO PULMONARY RESECTION
8 DERMAL GRAFT OF MAIN BRONCHIAL STENOSIS & LOBECTOMY IN PLACE OF PNEUMONECTOMY

Chart I.—Illustrates the fate of 136 patients with tuberculous tracheobronchitis, observed over a period of three and one-half years. The duration of disease varied from one to twenty years.

On the other hand, while personal experience, in man, with the use of dermal grafts for nontuberculous strictures, or for acute deformities resulting from the excision of malignant growths, is lacking, the applicability of dermal grafts in such instances should not be disregarded. A fibrous stricture of traumatic or nontuberculous origin may respond as well to a dermal graft as a healed, tuberculous stricture. In acute, traumatic, tracheobronchial defects, and those resulting from surgical excision, good results with dermal grafts might be expected, because they would be inserted in vascular, unscarred, normal tissues, and the adjacent respiratory epithelium would not be the loosely attached, atrophic and metaplastic membrane which lines healed, tuberculous stenoses. Usually acute, traumatic and excisional defects, in which partially intact cartilages persist, tend to gape and spread apart, rather than contract and close, as does an incised, fibroid stenosis. Nevertheless, the material used to fill such defects must have some semirigid support that will maintain a normal caliber of the trachea or bronchus. During the healing period, the contraction of such defects is marked, and a large defect is certain to form a stenosis if an unsupported graft is used.

Perhaps, in time, dermal grafts will be used more frequently for nontuberculous, tracheobronchial lesions than for the tuberculous type. For the present, however, until a better method is discovered and becomes available, their use is earnestly recommended for the latter, and their trial strongly urged for the former. It is felt that greater use of dermal grafts will lead to such a discovery, or to significant improvements in all the methods so far used.

In general, experience to date indicates that wire-enforced, dermal grafts are a good means of correcting severe stenoses of the major bronchi and trachea. As time passes, the anatomic results seem to improve. The clinical results are particularly good from the beginning, with a loss or reduction of obstructive symptoms, better aeration by roentgenogram, and an increase in measured ventilatory capacity. Practically all the patients have professed marked, symptomatic relief, and improvement in their respiratory capacity. The first four patients[1] are well and at home. Two are active housekeepers, one is working, and one convalescing. In each of these patients, upper lobectomy and dermal graft of a stenosed bronchus to the remaining lobe or lobes was performed. Three were sputum-positive before operation and are now negative; the fourth is still negative, as before surgery. (The seventh and eleventh patients had tracheal grafts and will be mentioned later.)

The remaining five patients had bronchial grafts. They are summarized for the purpose of illustrating postoperative complications, criteria for the selection of patients, and technical aspects of the operative procedure, so that others may utilize this experience.

CASE REPORTS

CASE 5.—T. T., woman, aged 31 years. In July, 1947, when first seen, this patient had been hospitalized for six years. Following unsatisfactory right pneumothorax, pneumoperitoneum had been used for three years. Wheeze and sputum block first occurred in 1942, after a right phrenic paralysis, which became permanent when repeated one year later. Bronchoscopy in July, 1947, disclosed a severely scarred larynx, and extensive, ulcerocaseous tuberculosis of the lower trachea and right bronchial orifice. Streptomycin therapy was started and three months later the patient was transferred to Leahi Hospital for right pneumonectomy. However, the sputum became negative, and completion of the healing process in the lower trachea and right bronchus was observed bronchoscopically, until a clean, healed stenosis of the right bronchus at the carina was the only residuum. Breath sounds were diminished to absent in the right chest. Slight cough and wheeze were the only complaints. The roentgenograms (similar to Fig. 1, *A*) had shown no change for a long time. Because of few symptoms, negative sputum, and unchanging roentgenograms, right pneumonectomy was considered unjustified, especially in view of the uninvolved middle and lower lobes. She was discharged on Sept. 25, 1948.

Two months later, repeat bronchoscopy revealed a right bronchial lumen approximately 1 mm. in diameter. Wheeze and cough had become more troublesome. The sputum was still negative and the right middle and lower lobes were roentgenologically clear. The patient was readmitted. X-ray studies disclosed a heavy, diaphragmatic stenosis of the right bronchus at the carina (Fig. 1, *D*), some dilatation of the distal right bronchus, and an atelectatic right upper lobe which appeared as a dense cap over the apex (Fig. 1, *A*).

Right upper lobectomy and repair of the right main bronchus seemed to be clearly indicated. At operation, on Jan. 26, 1949, excision of the stenosis and suture of the intermediate bronchus to the trachea, did not appear feasible; the gap resulting from excision would have been too wide. Right upper lobectomy was carried out, and a short, wide, diamond-shaped, dermal graft was applied to the incised stenosis. This was difficult be-

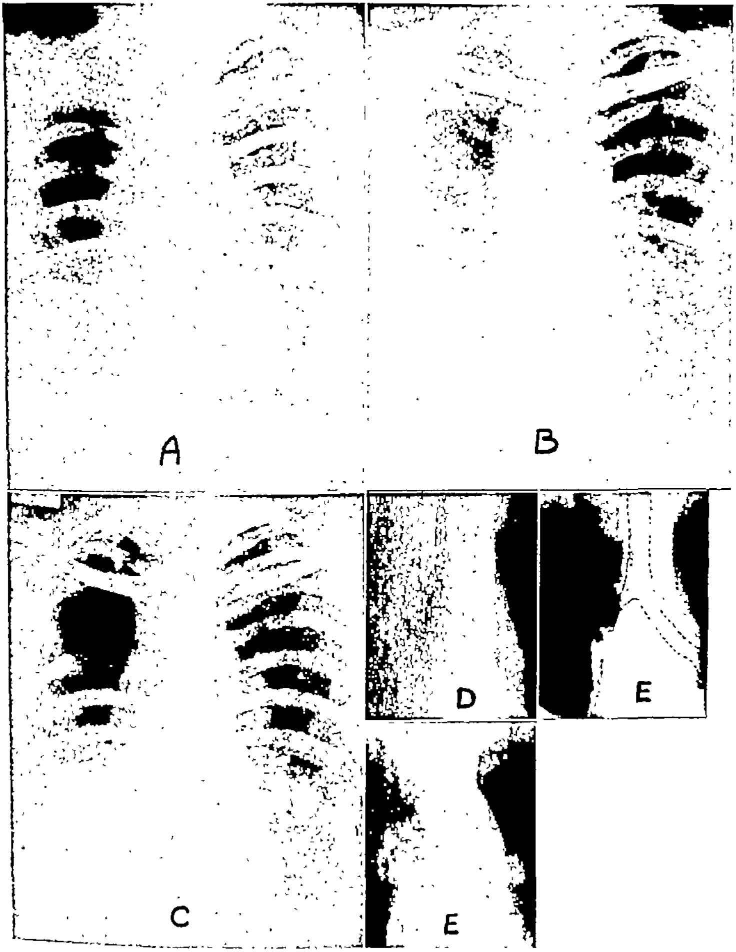

Fig. 1 (Case 5).—*A*, Before operation; permanent paralysis of right diaphragm, atelectasis right upper lobe. *B*, Five months after right upper lobectomy and dermal graft of right main bronchus. *C*, Eight months after operation, at time of discharge. *D*, Marked preoperative planigram. *E*, Marked and unmarked planigrams at the time of discharge.

cause of the nature of the stenosis. The short, heavy stenosis was hard to hold open. After being moulded to a round contour, the graft produced a large, posterior protrusion of the bronchial lumen, and the right bronchus was almost large enough to admit a finger. Postoperative recovery was entirely uneventful, except for hoarseness, secondary to laryngeal edema. Bronchoscopy, six weeks postoperatively, revealed a soft, edematous ring, 4 mm. in diameter, at the previous site of the stenosis. It was possible to worm the scope through it. The lumen beyond the carina was large, but the graft could not be identified. Everywhere the bronchial wall was smooth, clean, and pink. It is assumed that the stenosed portion of the bronchus pulled free from the graft, and attempted to reapproximate beneath it, with resulting recurrent stenosis. Planigrams (Fig. 1, *E*) showed the wire within the graft considerably posterior to the bronchial lumen. In the ensuing four months, six bronchoscopic dilatations were easily performed and a good lumen regained. Atelectasis did not occur (Fig. 1, *B*). Eight months after operation (Fig. 1, *C*), a clean, smooth, healed lumen, which admitted a bronchoscope with an external diameter of 7 mm., persisted, and the patient was discharged. No positive sputum cultures were obtained. One year after operation, the patient wrote, ''I feel better and breathing is lots easier than before. Climbing steps was pretty much of a strain for me before the operation, but now I find it so much easier, and don't get out of breath as I did before.''

Comment.—This fortunate result infers that it is not always necessary for a dermal graft to become a portion of the bronchial wall. Conceivably, it can function as a temporary seal of the enlarged airway, supply a framework, or scaffold for natural healing, and thus ultimately become an extrabronchial structure. However, such a method of bronchial repair is untrustworthy, and unappealing, the fortunate result in this instance notwithstanding. This case does exemplify the early tenacity of a dermal patch, for separation of the bronchus from the graft evidently did not occur until healing had progressed to an airtight state. It also demonstrates the healing and sealing qualities of the mediastinal structures.

It seems logical to conclude that, if possible, a short, weblike, or diaphragmatic stenosis should be treated by sleeve resection, as reported by Griffith.[4] The anxiety for a large airway encourages the use of wide grafts. The severity of the stenosis is proportional to the thickness of the bronchial wall. The thicker it is, the more it tends to curl back, and the harder it is to hold open. Too wide a graft produces undue transverse stretch on the bronchus; consequently the sutures cut through, as they do in all wounds closed with high tension, and the freed bronchial incision tends to reapproximate under the graft. It is probably better to err on the small side, rather than take this risk. Also, a small graft is more likely to take than a large one. On the other hand, when a graft fails to hold without complication other than the recurrence of stenosis, as in this instance, dilatations during the healing period may finally provide an adequate airway.

This patient is a good example of complete healing of an entire lobe by fibrosis and contraction, secondary to occlusion of its bronchus by healed scar. The clinical course of the upper lobe disease, and the gross and microscopic examinations of the removed lobe, indicated that it, alone, would probably never have caused trouble. The patient was reasonably well until the bronchial deformity reached a crucial point, productive of distressing symptoms, which arose from purely mechanical obstruction and were relieved by a mechanical procedure.

Case 6.—F. Y., woman, aged 28 years. Admission x-ray film (Fig. 2, *A*), in 1944, showed an elevated right hilus from which a dense wedge extended to the apex, and scattered infiltration in the sub-apex. Extensive, ulcerocaseous tuberculosis of the lower trachea and right bronchial orifice was discovered at bronchoscopy. Despite this, a right phrenic crush was done for a spread to the right base. Incredibly, the base cleared and the sputum became negative. After eighteen months, the lower trachea and right bronchus showed considerable healing. The patient was discharged in 1946, after two years of hospitalization. Six months later, a sputum culture was positive. No x-ray change was noted, and no other positive findings occurred during a second admission of one year. This case was regarded, erroneously, as a possible instance of healing of the upper lobe by fibrosis, secondary to bronchial occlusion, as was demonstrated in Case 5.

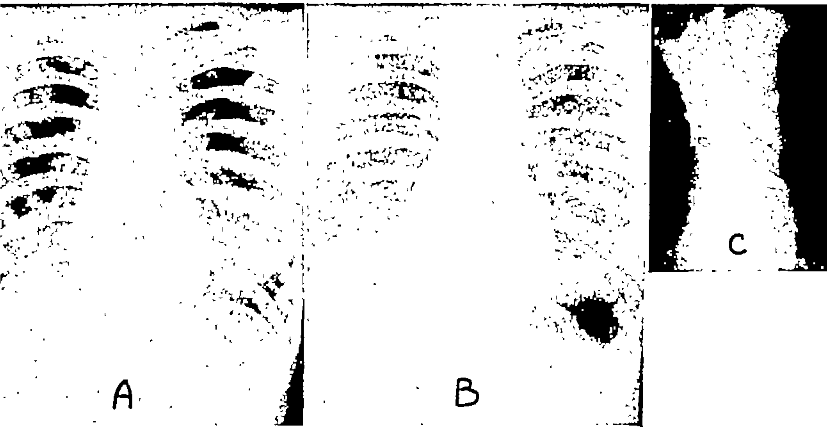

Fig. 2 (Case 6).—*A*, Admission roentgenograms, 1944; atelectasis right upper lobe, infiltration upper half of right lung field. *B*, Over four years later, just before operation; infiltration has cleared. *C*, Marked planigram before operation.

Six months after the second admission, increased wheeze and cough occurred, and the sputum became positive on smear. At bronchoscopy, the trachea appeared normal and there was a severe, healed stenosis of the right bronchus at the carina. There was no change radiologically (Fig. 2, *B*). Planigrams (Fig. 2, *C*) demonstrated probable occlusion of the upper lobe bronchus. Right pneumonectomy, or upper lobectomy and dermal graft of the main bronchus, seemed clearly indicated.

On Feb. 9, 1949, a dense, contracted, infiltrated and atelectatic, upper lobe was removed. No lumen could be demonstrated in its bronchus; active inflammation was later demonstrated by microscopic section. Opposite the upper lobe stump and at the carina, the opened right main bronchus had a lumen of 2 by 4 mm. There was no exudate; the lining was smooth, moist, and glistening. The middle and lower bronchi appeared normal, and both lobes were negative to palpation and inspection. A large, dermal graft was applied to the right bronchus.

The postoperative course was characterized by cough and a moderate bronchorrhea. Five months after operation (Fig. 3, *D*), the grafted bronchus seemed to be completely epithelized, and admitted a standard 7 by 40 bronchoscope. Shortly thereafter, the sputum became positive and there was evidence of fresh infiltration in the expanded right middle or lower lobes (Fig. 3, *E*). Sputum cultures were still sensitive to streptomycin; it was again administered, and PAS was added. By roentgenogram (Fig. 3, *F*), the infiltration in the lung cleared in one month, but cough and bronchorrhea increased; harsh breath sounds and rhonchi became audible over the trachea and mid-upper chest. Bronchograms and bronchoscopy revealed a recurrent, tuberculous inflammation of the trachea, characterized by minute ulcerations and heaped-up projections of caseous exudate, and a fairy large, caseous mass in the lower trachea, obstructing the orifice of the left main bronchus. Much of this was removed with biopsy forceps. On section, the removed fragments proved to be granulation tissue. No tubercles were encountered. The grafted right bronchus showed no gross involvement. After bronchoscopy, there was marked symptomatic improvement. The sputum converted to negative in three months, and has continued negative. Eleven months after operation, bronchoscopy showed practically complete healing but wire loops protruded into the tracheal lumen, just above the bifurcation, at the site of the previously-noted, caseous mass. Evidently, the recurrent tuberculosis had involved the tracheal portion of the graft. The wire loops were flattened with the tip of the scope; future cutting and removal were contemplated. A second, three-month course of PAS was started. One

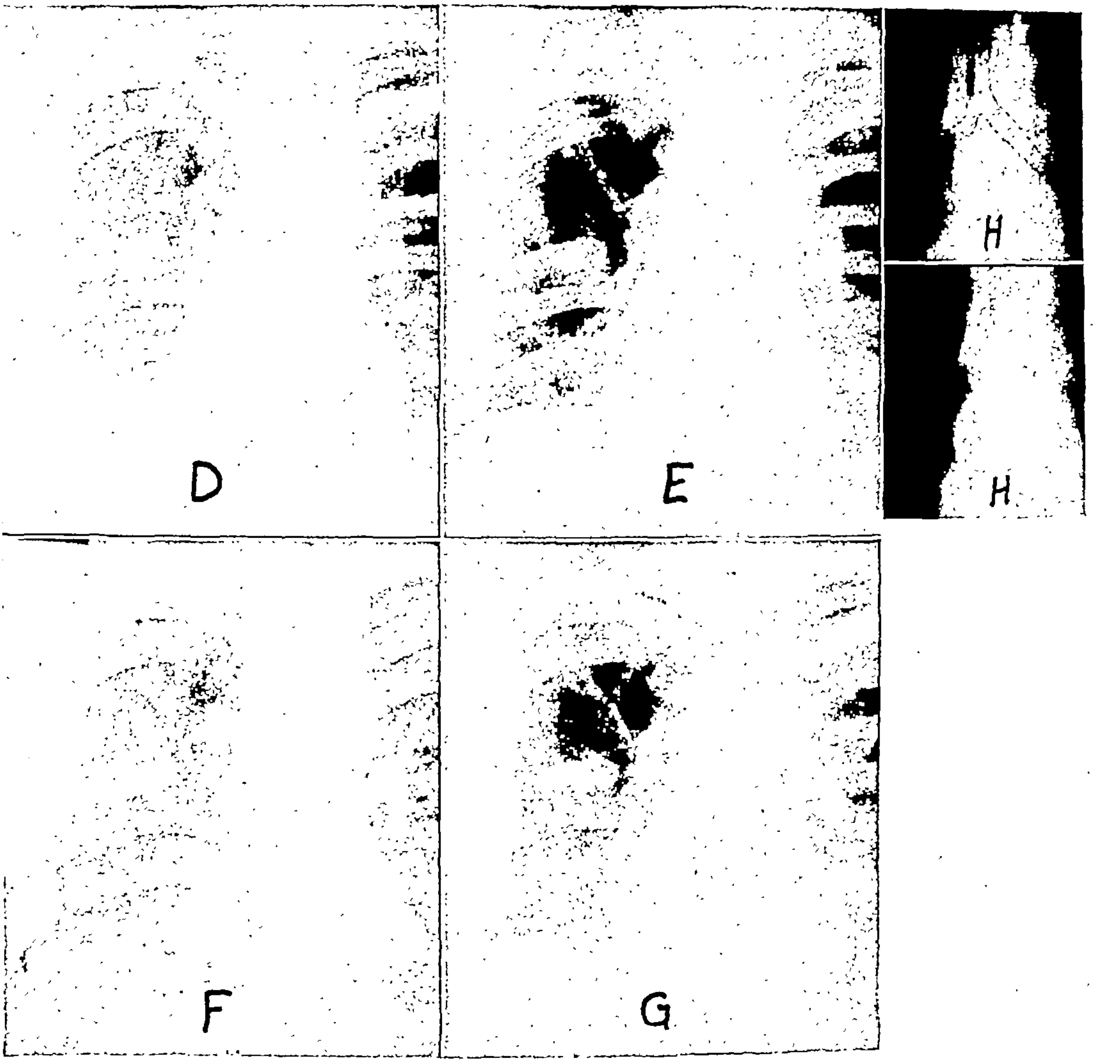

Fig. 3 (Case 6).—*D*, Five months after right upper lobectomy and dermal graft of the right main bronchus. *E*, One month later; fresh infiltration right upper lung field, recurrent, tuberculous tracheobronchitis. *F*, One month after *E*, six months after operation; clearing of infiltration (patient received PAS and a second course of streptomycin). *G*, Fourteen months after operation: sputum negative; good healing noted bronchoscopically. *H*, Planigrams marked and unmarked, at the same time. Bronchial lumen adequate. Wire within the graft was removed, bronchoscopically, eleven months after operation.

month later, in January, 1950, the protruding loops of wire were cut and removed through a bronchoscope, whereupon additional wire loops became visible through a thin, filmy covering in the posterior wall of the proximal right bronchus. With more courage than skill, the wire was grasped with forceps, and completely extracted by a steady pull. There was little bleeding, and the right bronchial lumen remained open and unchanged.

The second course of PAS has just been completed. Fourteen months after operation, the bronchus appears healed, an adequate lumen is present and the chest film (Fig. 3, *G*) is clear. The patient is well; there is some cough, and about two ounces of mucoid sputum per day, which is negative. Planigrams (Fig. 3, *H*) show an adequate bronchial lumen.

Comment.—The ultimate result in this patient probably will be most acceptable. More cough and sputum than in other cases was present from the beginning. Although atelectasis never occurred, five months after operation a light spread of the disease, and a rather severe, recurrent tracheobronchitis did. All in all, the postoperative course was the least satisfactory of this experience. The availability of PAS was most fortunate, and it must be given credit for the result to date.

The removed lobe showed atelectasis, bronchiectasis, tuberculous infection in various stages of activity, and severe fibrosis—an entirely different picture from Case 5. There are probably many patients harboring healed, fibrosed, atelectatic lobes or segments similar to that removed in Case 5, which represents the ultimate in natural healing. On the other hand, it is pertinent to realize that, in the absence of positive sputum, there is no clinical or radiological means of differentiating such a lobe or segment from the type removed in Case 6. A small, dense, atelectatic lobe or segment, visible in an x-ray film, particularly if influenced by past or present collapse, is far from acceptable evidence of healing. They are a frequent source of future trouble, and are best removed, if there is the slightest laboratory or clinical evidence of activity.

This case points out that, despite long duration and every clinical evidence of healing, smouldering inflammation may persist in a healed, tuberculous bronchostenosis, and that following a graft, it may flare up when the effect of protective medication wears off. Fortunately, it is not a common event, and is highly improbable in the late, postoperative months. It can be partially avoided by carefully selecting patients and remembering that tuberculous bronchostenosis usually requires pulmonary resection. The preceding case is evidence that recurrent infection cannot always be avoided, inasmuch as the indications for dermal grafts in this patient were unquestioned.

Certain general opinions regarding the selection of patients have been formulated from the experience to date. Naturally, their revision may be necessary in the future, as more grafts are done. Healed, tuberculous tracheobronchitis is a relative state. Histologic evidence of activity is not a criterion of clinical healing; it may be found in lesions known to be years old, yet difficult to find in other lesions which were ulcerocaseous only a year before. Such lesions rarely heal in less than one year, and they are the type that result in stenosis. It is better, therefore, to wait at least a year after gross evidence of acute, destructive inflammation, before considering a graft. The procedure should not be attempted hurriedly, solely for the purpose of avoiding extension of the pulmonary disease, or the development of bronchiectasis.

Bronchoscopically, a healed stenosis appears clean, smooth, moist, and glistening. It appears lined with epithelium and the color is practically the same as near-by normal structures. Hyperemia indicates residual activity, or stasis, with distal secondary inflammation. The latter usually signifies the presence of bronchiectasis which is best treated by excision. Unlike true, caseous exudate, dried secretions accumulated on a clean base may not contraindicate surgery. Ordinarily, a single, stenotic lesion is usually in a uniform state, but unsuspected, gross evidences of activity in the bronchial wall may be encountered at operation, which call for resection. Therefore, it is better first to open and inspect the bronchus distal to the stenosis, before extending the incision through it into the trachea. Thus, if a graft is contraindicated and resection carried out, a repair of the airway above the stenosis will be avoided.

In three of eight instances of dermal grafts to healed stenosis of main bronchi plus lobectomy, the bronchus of the lobe removed was the site of caseous destruction at the level it was first circumsected. In each instance, satisfactorily healed, fibrous tissue was present more centrally, adjacent to the healed main bronchus, and bronchial closure was easily accomplished. None of these patients had recurrent or subsequent infection, although it is highly probable that some active foci existed within these main bronchi. Only grossly discernible lesions, such as areas of soft granulation, or caseation, when found in the bronchus to be grafted, contraindicate the procedure. Their presence in the bronchi of removed lobes is common, and their discovery in a lobar bronchus, at operation, does not signify that a graft of a stenosed main bronchus should not be done, unless the process extends centrally into the main bronchus. Valuable practice and experience in the appraisal of gross changes in diseased bronchi can be gathered by careful observation of the divided bronchus at every pulmonary resection, and the study of fresh, surgical specimens.

The gross pathologic changes of the bronchus observed at operations are most helpful in choosing between resection and bronchial graft, in contrast to the findings which concern the lobe or lung. They will be discussed after the next case which is rather illustrative.

The remaining feature, illustrated by the preceding case, signifies that, if recurrent infection occurs, the wire within the graft is likely to be a nuisance. Once healing is complete, a skeletal framework in the graft, for the purpose of maintaining bronchial patency, is probably unnecessary. However, in the absence of infection, the wire is not likely to be harmful so long as it remains imbedded in the graft. Also, at the time of grafting, and during healing, the dermal skin needs support to hold open the repaired bronchus, and to provide an airway for the residual lung or lobes. It is felt that any absorbable material, used in place of the wire, would greatly diminish the chances of success with dermal grafts, because cellular infiltration is essential for absorption.

Twenty-eight gauge wire, originally used, is heavier than necessary, and 30 gauge has been found more satisfactory. A finer gauge than this mght be even better, especially if the incised bronchus can be held open easily. The smaller the wire, the easier it is to insert at a uniformly deep level in the graft. Kinks and irregularities are avoided more easily. If, after operation, cutting or removal of the wire should become necessary, it would be less difficult. Recurrent infection, as in Case No. 5, and placement of wire too near the epidermal surface, or the use of too heavy a wire which has irregular turns or kinks, and is difficult to mould properly, are the main causes for the postoperative appearance of the wire in the bronchial lumen. The periscapular skin of man is thick, and even after removal of the epidermis, the remaining dermal skin is frequently 3 mm. thick, or more, if it is not under tension. The inserted wire should be kept at least 1 mm. from the epidermal side. If the wire within the graft is visible through this surface, it is not deep enough. With wire no heavier than 30 gauge, the procedure is not difficult after a little practice. This is best done on fresh skin obtained from thoracoplasty patients. It is helpful to have the wire welded, in an "atraumatic" fashion, to a fine, cutting needle with a gentle curve.

CASE 8.—T. T., man, aged 30 years. In 1943, an army induction chest film showed a light, tuberculous infiltration in both apices, and more dense, scattered infiltration at the right base. Right pneumothorax produced atelectasis of the right lower lobe within nine months. It was discontinued and a right phrenic paralysis substituted. The sputum continued positive. Pneumoperitoneum was tried and abandoned because of severe wheeze. By January, 1945, the right lung had practically cleared and the right diaphragm resumed function. Shortly afterward, atelectasis and a massive spread occurred in the left lung, which increased initially, but, thereafter, never changed significantly. Bronchoscopy was first done in July, 1945, and showed "hyperplastic involvement" of both main bronchi. Early in 1948, a 120 Gm. course of streptomycin produced marked symptomatic improvement and converted the sputum for six months. There was no radiologic change. Bronchoscopy, in October, 1948, revealed hyperemia and occasional flecks of exudate in the right bronchus, and a healed stenosis of the distal left bronchus. The patient was transferred to Leahi Hospital for further study and possible left pneumonectomy.

There was exertional dyspnea. The left lung appeared to be destroyed (Fig. 4, *A*). Planigrams showed stenosis of the distal left bronchus (Fig. 4, *D*). The upper lobe bronchus could not be demonstrated. Sputum cultures were still sensitive to streptomycin. The patient's respiratory reserve was limited. Ventilatory studies showed a 1:1.7 ratio of tidal to vital capacities. They were 800 c.c. and 1,400 c.c., respectively. Bronchoscopy, in March, 1949, showed no change on the left, and the right appeared normal. Left pneumonectomy was advised only because an insignificant reduction in respiratory function was expected from removal of the diseased left lung.

At operation, on April 29, 1949, all the disease seemed to be confined to the upper lobe. The lower lobe was normal to inspection and palpation, and the fissure was practically free. The lower lobe did not collapse; it was compressed manually, and the upper lobe was removed. A short, fibrous, bronchial stump, in which a lumen could not be found, was sutured. Just distal to the point of division, the upper lobe bronchi were markedly dilated. The distal portion of the left main bronchus was then incised through the stenosis. It appeared healed and was lined with thin mucosa. Opposite the upper lobe stump, the lumen measured 3 mm. The left main bronchus, above the stenosis, contained a shallow, pouchlike, anterior protrusion, where the cartilages were intact. All the deformity of the stenosis was formed by the intrusion of the lateral and anterior bronchial walls. The appearance of the lower lobe branch bronchi did not suggest bronchiectasis; however, palpation now disclosed induration deep in the lobe, along the bronchovascular structures.

Ordinarily, such findings would indicate resection. In this case, it was felt that equally extensive induration probably existed in the right lung, because of previous disease visible in the early x-ray films. Also, a gamble for the function of a lobe seemed justified because of the patient's questionable preoperative respiratory function. Therefore, the left lower lobe was not removed, and the distal left bronchus was repaired with a dermal graft. A limited, modified thoracoplasty, designed to prevent overdistension of the remaining lobe, was carried out.

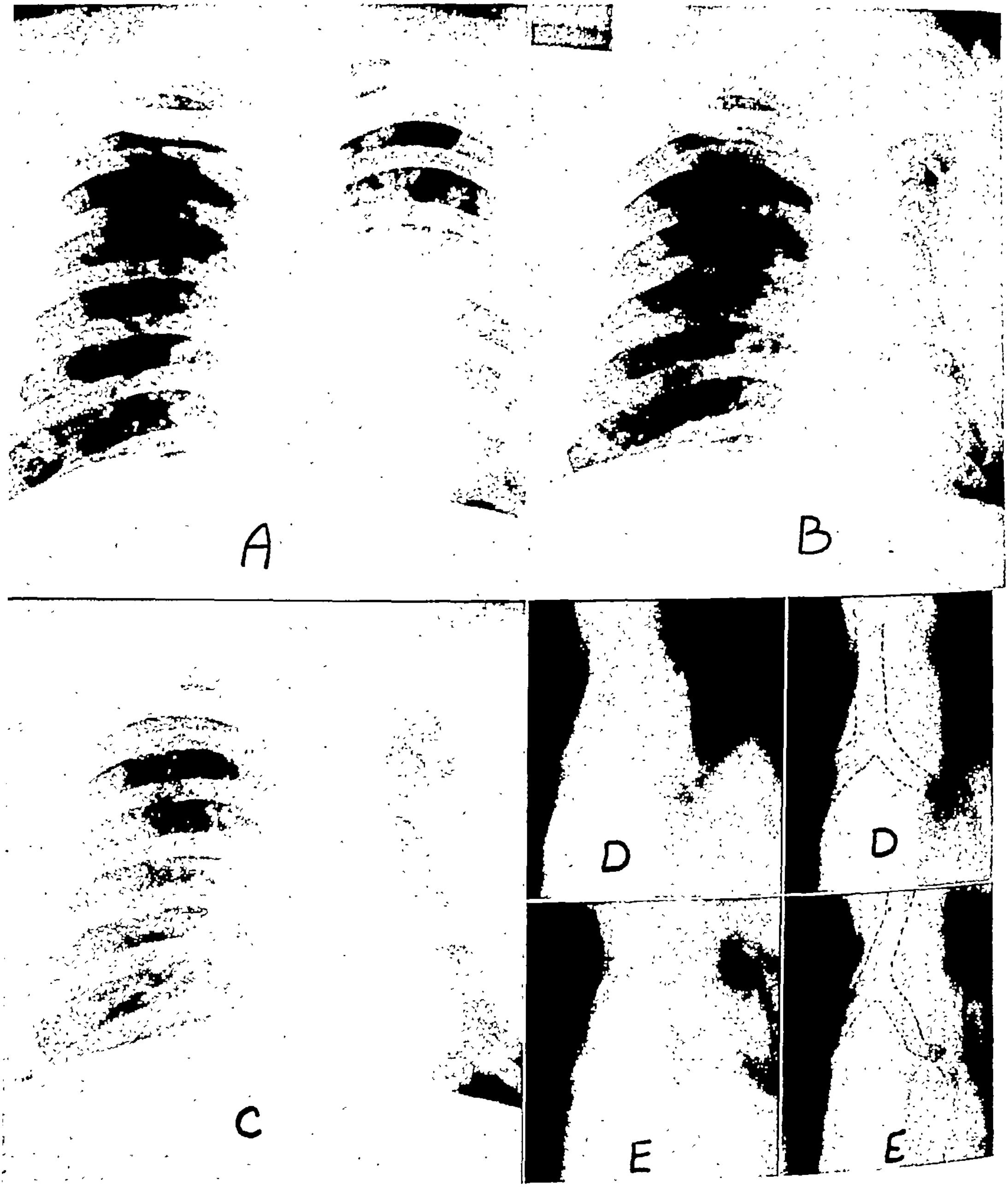

Fig. 4 (Case 8).—*A*, Before operation; extensive infiltration and density left lung, which proved to be entirely confined to the upper lobe at operation. *B*, Three and one-half months after left upper lobectomy, dermal graft of the distal left bronchus, and modified thoracoplasty. *C*, Eleven months after operation; sputum negative; recurrent, tuberculous bronchitis healing. *D*, Marked and unmarked planigrams before operation; severe stenosis of left bronchus in region of upper lobe orifice, which could not be demonstated. *E*, Planigrams eleven months after operation.

The early postoperative course was rather stormy. Good expansion of the lower lobe was slowly gained after the bronchoscopic aspiration of a mucopurulent plug in the grafted bronchus. One month after operation, a 7 by 40 bronchoscope was passed beyond the graft which appeared viable. Two months later it appeared to be covered with epithelium, except for a few, small, irregular, gray areas. The left lower lobe appeared clear in the x-ray film (Fig. 4, *B*). Breath sounds on the left were diminished. The heavily positive, preoperative sputum showed a "rare" bacillus in three of eleven concentrates, during the first three months. Since then, all examinations have been negative, except for one positive culture, six months after operation, which proved resistant to streptomycin. At this time, bronchoscopy revealed a fairly good lumen which admitted a standard 7 by 40 bronchoscope, but there were finely granular, hyperemic, irregular areas, and flecks of gray exudate, evenly distributed over the bronchial surface and the graft. No wire was visible. These findings were regarded as evidence of a recurrent, subacute, tuberculous or mixed infection, and PAS was instituted. Four months later, ten months after operation, there appeared to be satisfactory healing, but PAS is being continued to complete a six month course. There is a small amount of purulent sputum each morning, which contains staphylococci, but no acid-fast bacilli. There are diminished breath sounds at the left base and an occasional wheeze. The patient's general condition is excellent. There is very little cough and much less dyspnea on exertion. The lobectomy and modified thoracoplasty reduced vital capacity to 1,200 c.c., but the tidal air is now 450 c.c., and the ratio 1:2.6. Eleven months after operation, the left lower lobe appeared clear (Fig. 4, *C*), and planigrams showed a fairly good bronchial lumen (Fig. 4, *E*).

Comment.—For the present, this result is considered satisfactory; however, the ultimate result will not be known until sometime after PAS has been discontinued. It is felt that future lobectomy on the left might produce a respiratory cripple, and that such an event would certainly have followed pneumonectomy. In many clinics, no type of surgery would have been offered this case. Certainly, it would not have been intentionally selected for the trial of a new procedure in any clinic.

This experience establishes the fact that, even after careful preoperative study, unexpected operative findings may alter the preoperative intention. This should not be regarded an axiomatic "crutch," but evidence of the failure of preoperative evaluation. Every available means should be used beforehand, to determine whether or not the disease in the lobe or lung distal to the stenosis requires removal, for, at operation, simple inspection and palpation alone are not indicative of the extent or activity of minimal disease. Naturally, advanced or moderate disease is quite detectable, but so is it in preoperative roentgenologic study, and, in such instances, repair of the bronchus would not be contemplated.

In summary, before the possibility of a bronchial graft is considered, the bronchial disease must be regarded as healed, and the lung parenchyma distal to the stenosis considered entirely worth saving—either free of disease, or grossly cleared of previous involvement—without dense scars and healed nodules. A slight degree of bronchial dilatation, especially in the absence of infection, does not, of itself, contraindicate a bronchial graft, but its presence, added to other factors, might do so.

CASE 9.—O. A., woman, aged 50 years. Pulmonary tuberculosis began ten years previously, with positive sputum, cough, wheeze, and minimal pulmonary infiltration by roentgenogram. Left atelectasis and spread occurred in 1942, and acute, ulcerocaseous, tracheo-

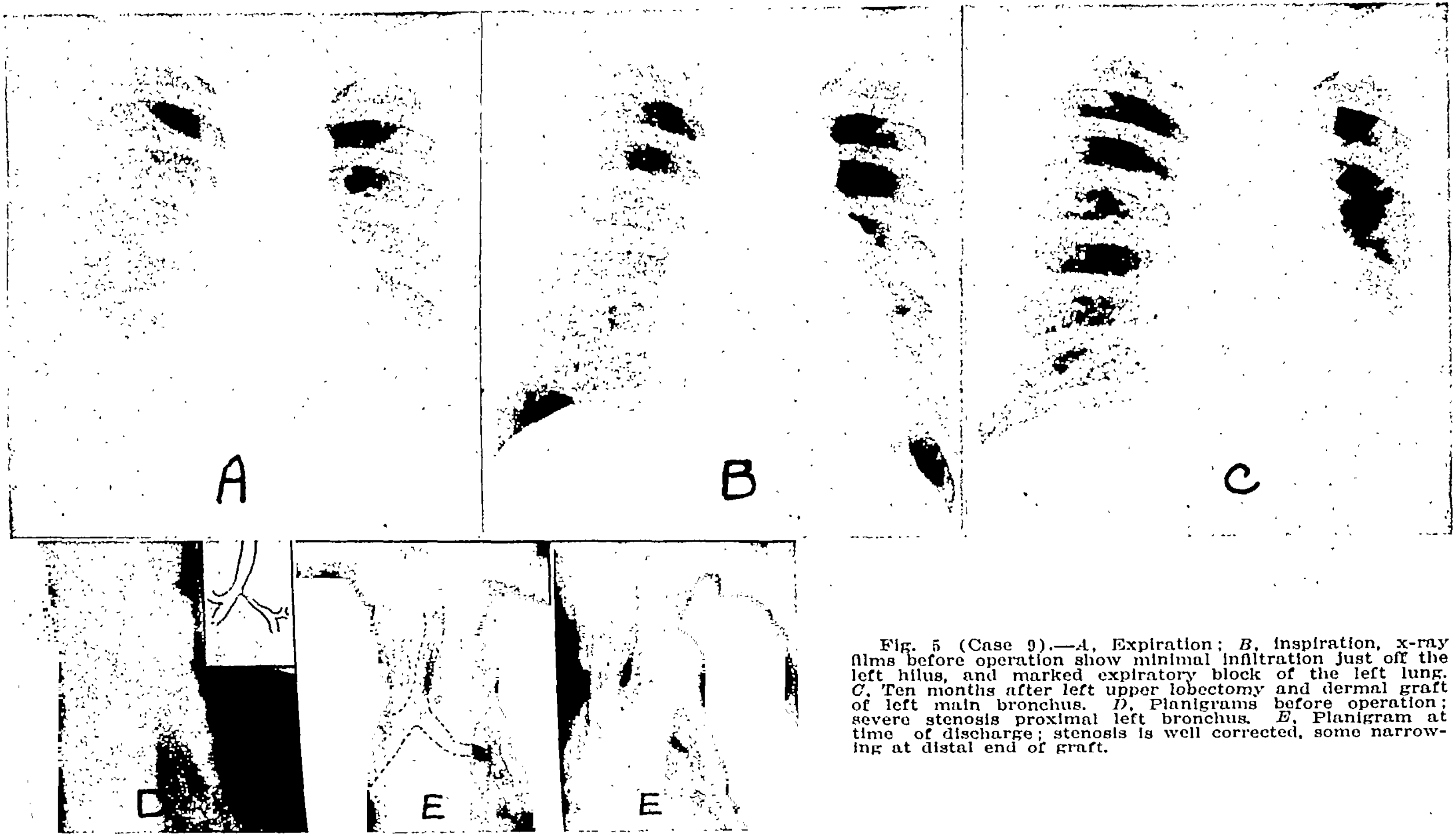

Fig. 5 (Case 9).—*A*, Expiration; *B*, inspiration, x-ray films before operation show minimal infiltration just off the left hilus, and marked expiratory block of the left lung. *C*, Ten months *after* left upper lobectomy and dermal graft of left main bronchus. *D*, Planigrams before operation; severe stenosis proximal left bronchus. *E*, Planigram at time of discharge; stenosis is well corrected, some narrowing at distal end of graft.

bronchitis was observed. A year later, severe stenosis of the proximal left bronchus was present, and the left lung had cleared, except for a residual patch of infiltration lateral to the hilus. Intermittent episodes of left atelectasis continued through 1943 and 1944. The mediastinum gradually shifted to the left. During 1945, the sputum was negative, the lesion in the left lung stable, and the left bronchus healed with a lumen of 3 mm. Lateral x-ray films located the infiltration in the lingula of the upper lobe. Throughout 1946, 1947, and 1948, the patient was observed closely in the out-patient department, and occasionally bronchoscopy was done. The general health was good; motion and breath sounds of the left chest were diminished, and a marked wheeze was audible. Cough was not a prominent symptom, but was usually necessary during the night to relieve tightness in the chest. The sputum continued negative. Re-evaluation, in 1948, decided against pneumonectomy, because of negative sputum, mild symptomatology, and the slight extent of the parenchymal disease (similar to Fig. 5, *B*). A series of bronchoscopic dilatations was advised. These had *no appreciable symptomatic effect, and actually reduced the bronchial lumen. Early in 1949*, the sputum became positive, and the symptoms increased considerably. Bronchoscopy and examination showed no change. There was no appreciable change in the x-ray films, and expiration-inspiration films showed a marked mediastinal shift (Fig. 5, *A* and *B*). Planigrams demonstrated the severe stenosis of the left bronchus and suggested a similar deformity of the upper lobe bronchus (Fig. 5, *D*). Dermal graft of the left bronchus and upper lobectomy was recommended, and performed on May 18, 1949.

The postoperative course was exceedingly smooth, with complete loss of cough, sputum, and wheeze. A feeling of tightness disappeared. Deep breathing was easier, and the patient was able to sleep through the whole night without coughing. Bronchoscopy, five months after operation, revealed a clean, healed bronchus with a practically normal lumen at the carina. Opposite the former site of the upper lobe bronchus, the lumen was oval in shape and measured approximately 6 by 4 mm. Postoperative planigrams (Fig. 5, *E*) showed a good bronchial lumen and a well-placed wire within the graft. Ten months after operation, she is doing her own housework and the left lower lobe is clear (Fig. 5, *C*). The mediastinum is still displaced to the left.

Comment.—One year before operation, this patient was told that the extent of disease, and the symptoms, did not warrant the removal of a lung. This opinion was not entirely satisfying, but the release from the prospect of a major operation was readily accepted, even on the terms of bronchoscopic dilatations. When the sputum became positive and symptoms increased, this patient, aware of the status of other patients who had received dermal grafts, was anxious to accept surgery. In general, this was an ideal case and a gratifying result.

The lingula of the removed upper lobe consisted of a fibrotic segment with dilated bronchi full of caseous material. The remainder of the lobe exhibited mild dilatation of the bronchi and a few, healed, tuberculous foci. There has been every indication that the lower lobe is practically normal. These findings are considered most unusual in the presence of a severe stenosis for seven years. Ordinarily, lung destruction would have progressed to an advanced state in a much shorter time. Perhaps the absence of significant infection is responsible. At least, the duration of a stenosis is not always an index of the degree of parenchymal damage.

The technical result lacks perfection only because of the oval, somewhat diminished, lumen at the distal end of the graft, somewhat beyond the original stenosis. This is likely to occur if a graft is not extended well into the normal structures above and below the stenosis. Tracheal extension is easy, but distal extension into the lower lobe bronchus is limited at the orifice of the superior segment, unless the bronchial incision is carried into this bronchus, and the graft inserted as a part of its lumen.

CASE 10.—K. M., woman, aged 49 years. Following hemoptysis, in 1945, this patient was admitted with a history of cough and wheeze for the previous year. Bronchoscopy revealed a moderately severe, healed stenosis of the left bronchus, beyond the carina. The admission roentgenogram is reproduced in Fig. 6, *A*. A marked wheeze was audible on the left. Despite this, pneumoperitoneum was started in October, 1946, and discontinued after one year, because of persistently positive sputum, cough, and wheeze. Shortly thereafter, the sputum became negative and gradual x-ray clearing ensued. In June, 1948, an ambulant status was assumed. In less than a year, cough and wheeze increased markedly, and the stenosis was found to have a lumen of 2 mm. in the mid-portion of the left bronchus. The status of the left lung (Fig. 6, *B*) was debatable. Planigrams (Fig. 6, *D*) showed no enlarged bronchi distal to the stenosis. During the previous twenty months, thirty-five three-day sputum concentrates had been negative, except for two questionable bacilli in February, 1949. There was no contraindication to left pneumonectomy, but the left lung was probably stable, and considered worthy of salvage.

At operation, on June 8, 1949, the pleura, including the fissure, was practically free of adhesions. The lower lobe seemed normal, except for some firm, central induration. Multiple, hard, small, discrete nodules were palpable in the upper lobe, most marked near the anterior surface of the lingula. Examination of the opened bronchus showed practically normal lobar orifices, no retained secretions, and a healed, severe stenosis in the distal two-thirds of the main bronchus. A dermal graft was applied to the stenosed bronchus, and no pulmonary resection was performed. Reactivation of the parenchymal disease was considered no more than a possibility. In that event, pneumonectomy could be done later.

On the second postoperative day, bronchoscopic aspiration of a mucous plug from the left bronchus was performed (the only instance, in the series, of bedside bronchoscopy). Thereafter, good aeration of the left lung ensued and persisted (Fig. 6, *C*). This patient no longer has cough, wheeze, sputum, or chest tightness, and feels that she can breathe much easier and deeper. The bronchial graft is completely healed and clean. The bronchus admits a standard 7 by 40 bronchoscope, however, the walls are soft and pliable and the lumen makes a noticeable posterior dip. Planigrams (Fig. 6, *E*) show a much improved airway and a well-placed wire in the graft. Except for one positive culture, six months after operation, all sputum examinations have been negative, as before.

Comment.—This graft was applied in the presence of definite parenchymal disease of uncertain stability, which, at the present time, ten months after operation, is certainly no more active than before operation, and symptomatic relief has been gained without removal of the lung. The one positive sputum culture is suspected to have come from the lingula. Perhaps resection of the upper lobe, at least lingulectomy, at the time of the bronchial graft, would have been better treatment. The answer depends on the future course of the patient. The fact that the operative procedure has not caused regression of the parenchymal disease is considered significant.

FATE OF THE GRAFT

The seventh and eleventh patients were operated upon primarily for severe, tracheal stenosis; both had marked stenosis of the right bronchus, in addition. They have been reported in detail.[2, 3] The latter died, probably because right pneumonectomy was performed at the time of the tracheal graft. The former had separate grafts applied to the trachea and to the right bron-

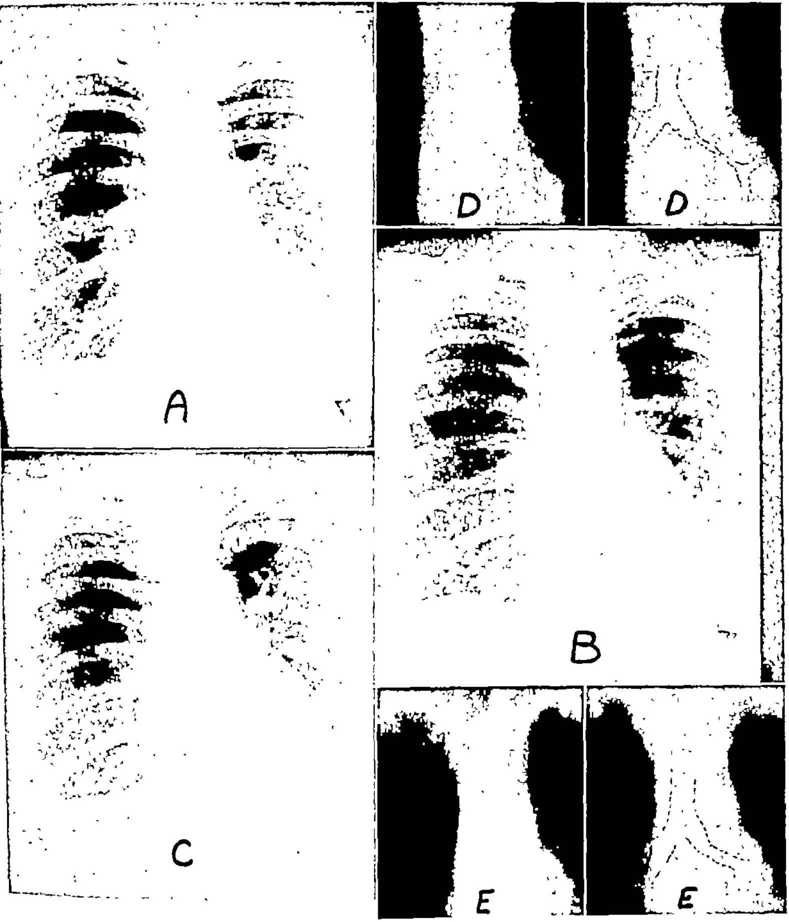

Fig. 6 (Case 10).—*A*, Admission roentgenogram, 1945: scattered infiltration both lung fields, more marked on left. *B*, Four years later: sputum negative, severe obstructive symptoms secondary to stenosis of left bronchus, shown in *D*. *C*, Nine months after dermal graft of left main bronchus; no pulmonary resection. If active disease persists, it probably is located in the left, second, anterior interspace, where the original disease was the most extensive. *D*, Preoperative planigrams, showing stenosis distal half of left bronchus. *E*, Rather poor reproductions of postoperative tomograms which did show a good bronchial lumen. The wire in this graft is perfectly placed. The loops are close together and their shadow is blurred by cardiac motion, during exposure. This diminishes the contrast between the bronchial lumen and the denser surrounding structures.

chus. The tracheal result was excellent; the bronchial graft was functionally adequate, with a lumen approximately one-half normal size. It led to aeration of atelectatic segments, not recognized before operation, which proved to be bronchiectatic, and responsible for symptoms requiring right pneumonectomy almost one year after the dermal grafts had been applied. This patient is now well and convalescing. A previous report[3] of this case contemplated resection, but the operative and microscopic findings have not been recorded.

At the time dermal grafts were first proposed for the reconstruction of stenosed bronchi,[1] the possibility was expressed that a dermal patch might act as a temporary seal of the enlarged bronchus, and supply a scaffold for natural regeneration and healing, rather than survive as a portion of the bronchial wall. Such a process is the only conceivable means of ultimate healing when the graft becomes detached from the bronchus, as in Case 5. Partial destruction of the graft by infection might also stimulate a similar healing effort, even though the graft in Case 6 apparently survived recurrent infection. On the other hand, in the absence of these complications, the evidence of Case 7 indicates the whole dermal patch survives as viable tissue, and becomes a living part of the bronchial wall, over the same area and exact location of its original insertion.

CASE 7.—On February 15, 1950, M. T., man, aged 35 years, had a right pneumonectomy performed, as stated previously, just two weeks short of one year after dermal grafts had been applied to both the trachea and the right bronchus.

The gross findings, at operation, exceeded all expectations. The grafted right bronchus was approached from the posterior aspect; the overlying lung separated easily from its posterior surface; the graft was exactly where it had been placed, most of the fine wire sutures being embedded and invisible. It was yellowish pink in color, and, except for the absence of cartilages, very similar in appearance to the adjacent bronchus. The line of union was indistinct, but discernible because the graft was somewhat thicker than the bronchial wall, and because an occasional tip of a wire loop within the graft, was visible at the margins of the graft, where it joined the bronchus. These short segments of wire were well covered with fibrous tissue. No wire was visible on the surface of the graft, which was smooth and exhibited a slight posterior bulge.

As previously reported,[3] ventilatory studies had demonstrated excellent function in this patient. The preoperative plan was right lower lobectomy, and possibly a wider graft in the right bronchus. The patient was also aware that pneumonectomy might be necessary. In order to inspect the lobar bronchi, and thereby gain more information regarding the necessary extent of resection, the bronchus was opened lengthewise through the graft.

The wire within the graft was completely embedded, and each strand was divided with scissors. The graft cut like skin, and seemed thicker than originally. The cut edge looked like freshly incised skin, with multiple, minute, bleeding points. The whole circumference of the bronchial lumen was smooth, moist, and glistening. It was pale and appeared to be lined with a thin, mucosal layer. From the bronchial lumen, the junction of graft and bronchus could not be identified. The middle and upper lobe orifices were thickened, and the spurs rounded. Each orifice was patent and approximately 5 mm. in diameter. Lower lobectomy was decided upon, with closure of the proximally opened bronchus, or an additional small graft. The opened bronchus was packed with moist gauze to prevent leakage of the anesthetic gases, and seepage of blood into the lobar bronchi and trachea. These structures were aspirated and the packing renewed a number of times during dissection and treatment of the lower lobe hilus. Although the procedure was necessary, it was done reluctantly and carefully, for the thin membrane, lining the bronchus, obviously was being removed.

With the main bronchus open and packed, the right lung was atelectatic, and differential lobar inflation was inapplicable. The lobar fissures were fused. During their difficult separation, the anterior segment bronchus of the upper lobe was inadvertently incised through the point of its division into three branches, where reunion by suture was impractical. Therefore, because of the somewhat questionable status of the middle and lower lobes,[3] pneumonectomy was done, rather than excision of the damaged segment.

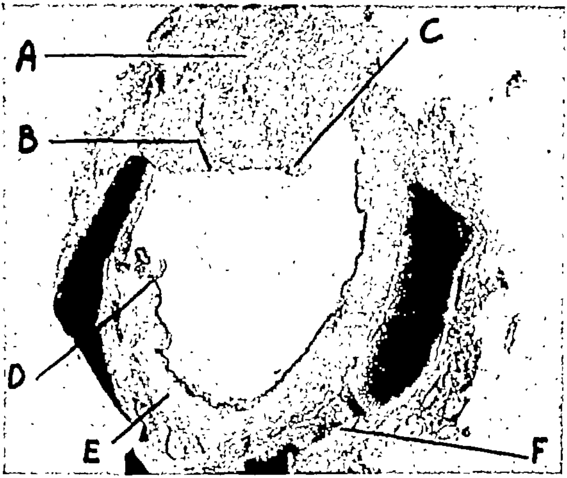

Fig. 7 (Case 7).—Transection of distal, right bronchus, taken near end of graft, approximately one year after original operation. *A*, Dermal graft, posterior wall of bronchus. *B*, Denuded surface toward the bronchial lumen shows no cellular infiltration. *C*, Basophilic granular material suggesting degenerating epithelium. *D*, Atrophic, bronchial epithelium. *E*, Severe fibrosis of bronchial wall. *F*, Healed, or regenerated, cartilage.

The removed lung exhibited no active tuberculous process, bronchiectasis of the middle and lower lobes—not marked in the former—and a small, recurrent, subpleural cyst in the upper lobe, plus fibrosis. Microscopic sections of the grafted bronchus (Fig. 7) disclosed bronchial fibrosis without absolute evidence of tuberculosis. On the side of the bronchial lumen, the dermal graft had no epithelial covering, and the absence of surface, cellular infiltration indicated that something had been removed. In some sections there were folds and recesses of the dermal surface. In these areas, a granular, basophilic material covered the derma. It could not be identified, but suggested degenerated, nuclear fragments, possibly residual, squamous epithelium. In isolated areas, remnants of a bronchial type of epithelium were encountered which may have been displaced from the dermal surface. In a few, small fields, simple, cuboidal epithelium covered the derma.

In one longitudinal section, near the junction of the graft and bronchus, an island of growing cartilage was observed, possibly representing regeneration of cartilage toward the graft, if not into it.

Dr. I. L. Tilden, consultant pathologist, made special stains and studied the sections. A portion of his description follows: "The dermal graft, itself, was composed of normal-appearing, collagen bundles, containing several groups of sweat glands, and in one preparation, a pilo-sebaceous apparatus was present. The sweat glands were lined by well-preserved epithelium and appeared entirely normal. Verhoeff's stain showed a normal elastic tissue pattern, and various collagen stains showed no deviation from normal on the part of the collagen bundles, except a tendency toward hyalinization in isolated areas."

Apparently a dermal patch, sutured into a bronchial defect, with one surface exposed to the air passage, survives, with little change in its elastic and collagen elements.

Concerning the preservation of these elements, viability of the graft, and the disappearance of sebaceous and hair-follicle structures, the findings in the preceding case are the same as the histologic observations of Peer and Paddock,[5] who studied dermal implants in subcutaneous tissue. On the other hand, they found that after one year, the sweat glands appeared to be in a process of degeneration and replacement. In addition, retained fragments of epidermis survived long, and produced microscopic, cystic structures, and granulomatous areas. In the preceding case, the sweat glands do not show such changes, but appear diminished in number, and the only suggestion of epidermal structures are occasional areas of granular, basophilic material on the dermal surface. Also, the distribution of the collagen bundles and elastic tissue strands is practically normal. They do not appear contracted, and coiled up, as in the case of implanted derma.

Despite the scarcity of dermal covering in the sections studied, it is felt that some sort of epithelium existed that was removed during the operation. In other patients, the bronchoscopic appearance of grafts suggests an epithelial covering after a few weeks, which later becomes grossly indistinguishable from adjacent bronchial epithelium. It is felt that the removal of a good thickness of epidermis, at the time the graft is made, encourages an ingrowth of bronchial epithelium, and that residual areas of squamous epithelium eventually degenerate. If considerable squamous epidermis is present on the graft, it is likely to survive as such, at least, for some time. This is not entirely objectionable; however, ciliated bronchial epithelium would be ideal. Perhaps with the passage of more time, such favorable changes will occur.

It seems illogical to expect more normal epithelium than that which covers a healed stenosis. Nevertheless, studies of such bronchi in surgical specimens usually reveal a thin, loosely attached, atrophic type of bronchial epithelium, and a scarcity of mucous glands. Frequently the epithelium covers dense, avascular, scar tissue, which appears much less suitable as an epithelial base than a viable dermal graft.

Regardless of the ultimate type of epithelium covering a dermal graft, the absence of cilia should not be an objection to the procedure, for the graft only increases the bronchial circumference; it does not change or remove the epithelium which previously lined the bronchus, and ciliary action over a part of the bronchial circumferences should persist.

CONCLUSIONS

Until a better method is discovered, the judicious use of wire-enforced dermal grafts for the reconstruction of tuberculous tracheobronchial defects will salvage healed or disease-free lung tissue, destined for destruction by such defects. At the present time, there is a significant need for such a procedure in the treatment of tuberculosis. This need may be diminished by modern treatment, but it is likely to continue for some time. In addition, the method should be considered in the treatment of other tracheobronchial defects, for it is regarded as superior to the use of fascia, foreign body tubes, tantalum gauze, and other substances. In all probability, a more general use of wire-enforced dermal grafts will lead to an improved method, or the discovery of a better procedure.

Histologic and anatomic evidences, plus clinical results to date, indicate that dermal skin actually fulfils all the proposed requirements of bronchial grafts enumerated in a previous publication,[1] and survives as a highly suitable portion of the bronchial wall. Ultimately good clinical results may be obtained, despite the occurrence of complications, such as partial separation of the graft from the bronchus, and recurrent tuberculous infection.

The success of tracheobronchial dermal grafts depends on many factors, as illustrated by the reported cases. They include numerous features of operative technique and judgment, careful preoperative evaluation of the tracheobronchial defect and the parenchymal disease in each lobe, the application of resection whenever indicated, and the avoidance of its substitution by a dermal graft. Other factors are a meticulous preparation of the graft, the use of fine wire for its framework and sutures, abstention of tension caused by grafts of too much width, extension of the graft beyond the stenotic area, and the precise use of antibiotics before, during, and after operation. The use of early ambulation, physiotherapy to promote lung expansion, and the maintenance of an adequate airway are important postoperative measures, as well as the preservation of fluid, blood, and nutritive balance.

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DISCUSSION ON "THE EXPERIMENTAL USE OF HOMOGENOUS TRACHEAL TRANSPLANTS IN THE RESTORATION OF CONTINUITY OF THE TRACHEOBRONCHIAL TREE" BY DR. TRUXTON L. JACKSON, DR. E. J. O'BRIEN, DR. WILLIAM TUTTLE, AND DR. JOHN MEYER;* "RESECTION OF THE TRACHEA AND BRONCHI" BY DR. MAX G. CARTER AND DR. JOHN W. STRIEDER;† AND "FURTHER EXPERIENCES WITH DERMAL GRAFTS FOR HEALED TUBERCULOUS STENOSES OF THE BRONCHI AND TRACHEA"

BY DR. PAUL W. GEBAUER

DR. ANDRE JUVENELLE, Paris, France.—I should like to thank The Association for the privilege of discussing the valuable contributions of Dr. Jackson, Dr. Carter, and Dr. Gebauer and their co-workers. I must also express my gratitude to Dr. John D.

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*See page 598 for article by Jackson, O'Brien, Tuttle, and Meyer.

†See page 618 for article by Carter and Strieder.

Stewart, who has made it possible for me to work this year in his department at the University of Buffalo Medical School, with the constant collaboration of Dr. Coleman Citret. Our work has been along similar lines. I have enjoyed these papers very much, and it is now with a feeling of how small and inadequate our knowledge is on this subject compared with the large experience of the speakers that I would like to make the following remarks.

When Dr. Citret and I became interested in this field of investigation we were unfortunately not aware of Dr. Jackson's work published in October, 1949, in THE JOURNAL and our approach to the problem has been somewhat different from his. Our first experiments consisted of severing the right or left main bronchus, closure of the proximal bronchial stump, and reimplantation of the bronchus 2 or 3 cm. higher in the trachea through a window cut in the tracheal wall. After several failures due to difficulties with the anesthetic technique we succeeded in carrying out the procedure on five successive dogs, all of which had uneventful recoveries.

(Slides.) These slides illustrate the essential features of the anastomosis. The dogs were not given any antibiotics. They were followed by fluoroscopic and bronchoscopic examination at various intervals. It is naturally too soon to draw final conclusions, but the animals apparently show good healing and pulmonary function. The longest follow-up at present is four months. We are well aware that by this technique the tracheobronchial anastomosis was effected by sutures under considerable tension. This was deliberate, since it was felt that (1) conditions encountered in patients might necessitate removal of tissue and creation of defects which would have to be closed with some degree of tension unless prostheses or grafts were to be considered; and (2) this method was also used as a trial technique in preparation for attempts at resection of the entire tracheal bifurcation and reconstruction without prosthesis.

Our next experiments attacked this problem. The distal three or four rings of tracheal cartilage, along with the entire right main bronchus and similar length of left main bronchus was resected. Reconstruction was done by performing an end-to-end anastomosis of the distal end of the trachea and one of the main bronchi, then reimplanting the other main bronchus higher on the trachea, as described in the previous experiment. Two main obstacles were encountered: (1) adequate anesthetic apparatus and methods to maintain oxygenation throughout the procedure (the solution of these difficulties will be reported at a later date); and (2) tension at the suture lines due to the large defect. Attempts were made to elongate the trachea by making opposing partial circumferential incisions and covering the defects with fascia lata grafts. In our hands this method did not prove feasible. Then, somewhat to our surprise, we found that by freeing the trachea superiorly from its surrounding tissues in the mediastinum, it was possible by simple downward traction to bridge the defect and carry out the anastomoses.

(Slides.) These slides illustrate the resection and anastomosis. The procedure has been carried out on six dogs to the present time. Four have survived and are apparently well. One death on the ninth postoperative day showed good healing of the anastomoses at autopsy, the cause of death being distemper which was rampant in our kennel at that time. The sixth dog, which died on the third postoperative day, died during attempted functional studies. In carrying out these experiments pulmonary functional studies with the bronchospirometer and chemically induced bronchospasm have been done both pre- and postoperatively. Time does not allow a discussion of the results of these studies.

In conclusion, I have found the papers given today to be of great interest because I feel that a combination of grafts and transplants together may furnish answers to many unsolved problems in this field.

DR. ORLAND DAVIES, San Francisco.—During the past year, work has been in progress in the experimental surgery laboratories at the University of California School of Medicine, on homologous tracheal grafting in dogs. Sampling experiments were done with eleven animals to test the efficacy of various methods of preservation of tracheal grafts.

Although tracheal grafting procedures done without internal support were well tolerated in the immediate postoperative period, stenosis at the site of grafting occurred in all instances regardless of the method of preservation of the graft.

A technique was then developed whereby stenosis at the site of grafting was avoided by the use of a plastic (acrylic) tube used as an internal support for the tracheal graft. This procedure was used successfully to place grafts in the cervical and thoracic trachea in fourteen animals. These animals have remained free of respiratory difficulty two to six months after tracheal grafting. A similar method has been used to bridge defects formed by removing the distal trachea, carina, right lung, and a portion of the left main bronchus. Two animals in which the latter procedure was done have survived for two weeks and six weeks following the pneumonectomy and tracheal grafting procedure. This work will be completed and submitted for publication in the near future.

DR. F. J. JARVIS, Seattle.—I should like briefly to further the discussion of these excellent papers by presenting an attempt at replacement of the mediastinal trachea in man. In the first slide we will see a tracheogram of a man aged 33 years, who presented himself to me three days before I left for the St. Louis meeting of this Association, having had for twenty-two months symptoms of cylindroma of the trachea, and for eighteen months had had, on three occasions, endoscopic fulguration down to beneath the mucosal level.

(Slide.) In the tracheogram you will see the defect, representing the tumor which endoscopically appeared to be obstructing the trachea for about two-thirds of its lumen. The man was incapacitated almost wholly by the tracheal obstruction. I was stimulated by Dr. Daniel's report at that time, and also by a slap on the back from Dr. Berry, to return and attempt to excise the lesion.

(Slide.) You see here the artist's conception of the method used; the sternal splitting incision. The trachea was dissected free and 4 cm. of the trachea were removed and the trachea was replaced by a stainless steel tube. We selected stainless steel because of the difficulty in the wilds of Seattle of obtaining a Vitallium tube, and also its expense—when one considers that I had to make up several tubes not knowing which one I would use. This is a very simple tube and proved to be in this case at least temporarily satisfactory.

(Slide.) One sees here the tumor. You will observe that the tumor is obstructing the trachea markedly. It is a cylindroma although it has totally destroyed the wall and is invading the surrounding structures, but at this time it has not metastasized. I should prefer to call it an adenocarcinoma Grade 1, rather than a cylindroma which, as we know, is a metastasizing tumor, although metastasis occurs rather late.

(Slide.) You see the film taken on the tenth postoperative day, two days before the patient left the hospital. The tracheotomy was life-saving in his case, in order to evacuate secretions. He was gradually able to overcome this difficulty, and the tracheotomy was removed immediately after this film was taken and he left the hospital.

(Slide.) This film was taken a year later, with the tube still in place. The man has been working during this period, the operation having been performed in June, 1947. At this time the patient was perfectly well, and then I made my fatal error. Relying upon the previous experiments as related by Dr. Daniel, in which a rigid trachea was shown in dogs to have been regenerated surrounding these tubes, I removed the tube. The trachea that had been regenerated was sufficient to handle this patient for three weeks, but it was not because of stenosis that I was forced to replace the tube, it was because the patient, during cough, had not a sufficiently rigid trachea to handle it. He handled quiet inspiration and quiet expiration quite satisfactorily.

(Slide.) This is the tube which has not been cleansed, which has been in the trachea for thirteen months. Unfortunately, I do not have the slide which shows the lumen of the tube. It looks as if it had been taken out and scrubbed daily. The cough reflex was sufficient to keep it clean.

The unfortunate thing is that within three weeks I had to replace this tube and at that time there was a shadow in the upper right pleural cavity; there was also an adenoma of the left bronchus. Shortly, the patient began to show metastases.

I have unfortunately not the slide showing the autopsy specimen thirty-three months after the initial operation, in which there was generalized pulmonary and pleural metastases. Suffice it to say that in this one case the method seemed to be adequate, and had I left the tube in I am sure the patient would have been comfortable for a much longer time.

DR. W. E. BURNETT, Philadelphia.—I hesitate to prolong this discussion, yet these excellent papers are so stimulating that I want to present briefly some information we have obtained in the laboratory in the last two years. Dr. Robert M. Bucher and Dr. George P. Rosemond have done most of this work. We wanted to get something that would be easily accessible, that would be cheap, that would have rigidity enough to be molded, that would have a benign influence on the surrounding tissues, and therefore chose stainless steel wire mesh and performed some experiments on these dogs.

(Slide.) First, the tracheal ones, in which between four and six cartilages were removed, of the complete circumference after the first one in which partial circumference was utilized; the wire mesh was then placed overlapping the unopposed ends and sutured to the trachea with wire sutures. These two examples were sacrificed after five and six months, showing a considerable amount of epithelization, though still some granulations persisting, showing a good lumen with no evidence of stenosis. Unfortunately, they were not very carefully supervised, and we found that the animal house man had decided not to vaccinate against distemper, which had been our habit, so we lost two of these from distemper, one from massive infection, and one from too much anesthesia, out of ten dogs. However, those that survived the immediate period had an uneventful course until sacrificed.

(Slide.) It was difficult to make sections of these sacrificed specimens because of the incorporated wire, but by peeling off some tissue one can see that there is some degree of regeneration of cartilage as well as the lining membrane.

(Slide.) In the thoracic trachea, additional attempts were made but the mortality was quite high because of the same errors which I mentioned, plus inadequate amounts of antibiotics or attempts at mechanical removal of air in the chest due to leakage which occurred after a matter of three to five days, although skin grafts and pericardial grafts were used to reinforce the wire mesh which was the basis. Here is an example of a specimen four and one-half months after survival and sacrifice, in which one can see some of the wire mesh showing through by transillumination, although it has a slight covering of epithelium; it is infiltrated with tissue and was airtight. This dog had only a partial defect, as you see, rather than a complete circumferential one. Good regeneration of cartilaginous rings is demonstrated.

(Slide.) This is another slide of the inside, showing the wire mesh infiltrated by tissue but with incomplete covering; the edges, however, are well epithelized after about three months.

(Slide.) This is the outside view of the same specimen. This method gives promise and warrants further investigation. We are continuing the study.

DR. C. L. HOLMES, Boise, Idaho.—I, too, am reluctant to prolong this discussion but I think it is appropriate at this time to report a clinical case. About July 4, 1949, a man was taking off in his privately owned plane and crashed, and apparently received some injury to the midcervical region. He was admitted to the hospital several hours later, complaining of pain in the neck, some shortness of breath, and after a little time became cyanotic and apneic. An emergency tracheotomy was done by his local doctor and resuscitation was effected. Ten days later, the doctor opened his neck, explored this region, and found three cartilagenous rings crushed. These were removed in toto and an end-to-end anastomosis was effected with silver wire. A proximal tracheotomy was added through this area and ten days later the tracheotomy tube was removed. The stenosis was prompt, the patient was in considerable difficulty and the doctor could not reinsert the tracheotomy tube, and I was called. A dilatation through the tracheotomy wound was effected and the tube was reinserted. This was left for three months, then removed, and after a week or so the trachea began to stenose again, the patient was having dyspnea with exercise, and was raising considerable amounts of mucus. Being familiar with Dr. Jarvis' case, and the work of Dr. Clagett and Dr. Grindlay, I felt that some type of prosthesis should be used. A Vitallium tube three-fourth inch in length was constructed with a flange at each end with multiple perforations around it, and the stricture was dissected out and removed completely. Each end of the trachea was then sutured directly to the end of the tube. This was quite effective in relieving the patient, but about a month later he again noticed that he had difficulty in raising mucus. Bronchoscopy was done, a 9 mm. bronchoscope was dropped through the area without any difficulty, there was no stricturing tendency, but there seemed rather to be redundancy of mucosa at each end of the trachea. Dilatations were done periodically with the bronchoscope every one to two weeks for two or three months.

A month ago we went back into the neck and removed the original Vitallium tube and reinserted a one and one-eighth inch stainless steel tube completely within the trachea, projecting ½ to 1 cm. into the cricoid ring and into the distal trachea. On bronchoscopy just before leaving for this meeting, there was a complete airway, complete freedom of respiration with exercise, and we hope this will be effective in relieving him permanently. However, I felt that perhaps that was true with the first tube.

DR. STRIEDER (closing).—Many of you are familiar with Rob and Bateman's article in the October, 1949, *British Journal of Surgery*, in which they described the use of tantalum gauze covered with fascia to effect a repair of the cervical trachea. Their partial tracheal resection was for a recurrent carcinoma of the thyroid and included about six rings and the cricoid cartilage. They bridged the tracheal defect with tantalum gauze covered with fascia. Their difficulty was that they noted inspiratory stridor due to flutter of the free lining of the tantalum gauze tube, and overcame it by fulgurating the lining to create point adhesions. In our laboratory experiments we noted a similar difficulty and overcame it preoperatively by using interrupted sutures to fix the lining to the gauze. They also noticed emphysema in the neck and I presume, although the discussors did not mention it, that it was a complication of some of these repairs of cervical tracheal defects. The difficulty with tantalum gauze, in our experience, is that unless there is left a narrow rim of the posterior tracheal wall for suture purposes, obtaining an airtight closure posteriorly is almost impossible. In the thoracic trachea this would, and did in our cases, result in tension pneumothorax.

It is our impression that repair of the cervical trachea is easier than the thoracic trachea for reasons that have been stated by the discussors, and also because of the contiguous structures that buttress the suture line and tend to seal it more effectively.

THE TECHNIQUE OF PULMONARY DECORTICATION AND PLEUROLYSIS

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INTRODUCTION

THE recent war revived interest in the operation of pulmonary decortication and firmly established its value in the treatment of clotted hemothorax and its complications.[1-6] Impressive results in new applications[7-15] of the procedure have rapidly followed the military experience. In the numerous articles that are currently appearing in the literature, the matter of operative technique is given, for the most part, only passing consideration. The purpose of this article is to consider this phase of the subject and to emphasize the importance of pleural adhesions in the production of the pulmonary collapse. A modification of the usual operative technique will be described which has been used during the past two years in a group of patients requiring decortication for a variety of indications. This technique has substantially reduced the time required for the operation, the blood loss, and more importantly, has minimized injury to the lung.

GENERAL CONSIDERATIONS

It is not the intent of this article to consider the etiology, the various indications for operation, or to discuss the factors inherent in the collapsed lung[16, 17] which influence the operative result. We are concerned here entirely with operative technique and benefits that can be anticipated in patients properly selected for this procedure. Regarding this entire group, several generalizations can be made. The lung is maintained in its collapsed state by (1) the contents of the pleural space (air, blood clot, fibrin, fluid, or pus), (2) the peel, (3) pleural adhesions between the lung, chest wall, pericardium, diaphragm, and mediastinum.

Each of these factors is not equally important in maintaining the lung in its collapsed state. In the development of the pathology, collapse of the lung by hemothorax or pneumothorax occurs first, following which the peel and pleural adhesions develop simultaneously. For practical purposes, centripetal collapse never occurs, the lung being merely compressed toward the mediastinum (Fig. 1). The pleural adhesions thus form after various degrees of pulmonary collapse have already occurred. Their role in the pathology is directly pro-

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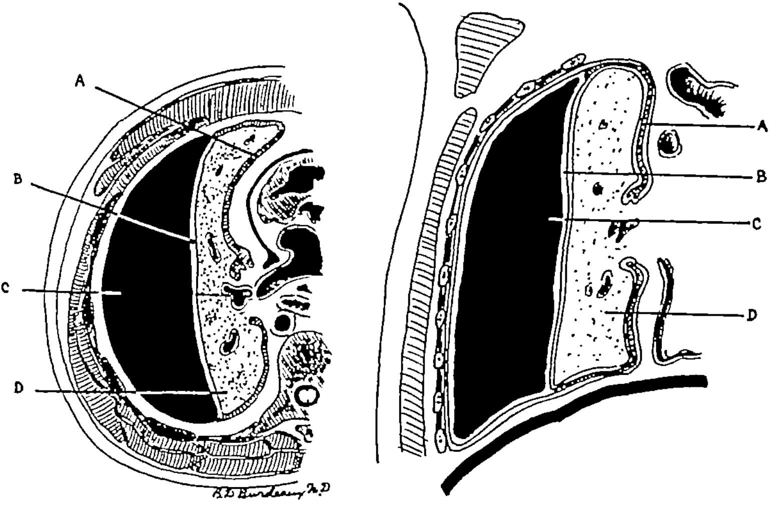
portional to the degree of compression and for this reason, division of these adhesions becomes an increasingly important part of operative treatment in those having extensive pulmonary collapse.

The peel maintains collapse in a different way. It is approximately the same in size in those patients having comparatively small as well as those having more extensive degrees of pulmonary compression. The importance of its role in maintaining the collapse appears to be directly proportional to the area of the lung which it covers and is inversely proportional to the degree of pulmonary collapse. In short, it appears correct to state that the lung is compressed by the pleural contents, it is imprisoned by the peel, and restrained by the pleural adhesions. This concept of the surgical pathology, as will be shown later, has important practical application in operative treatment.



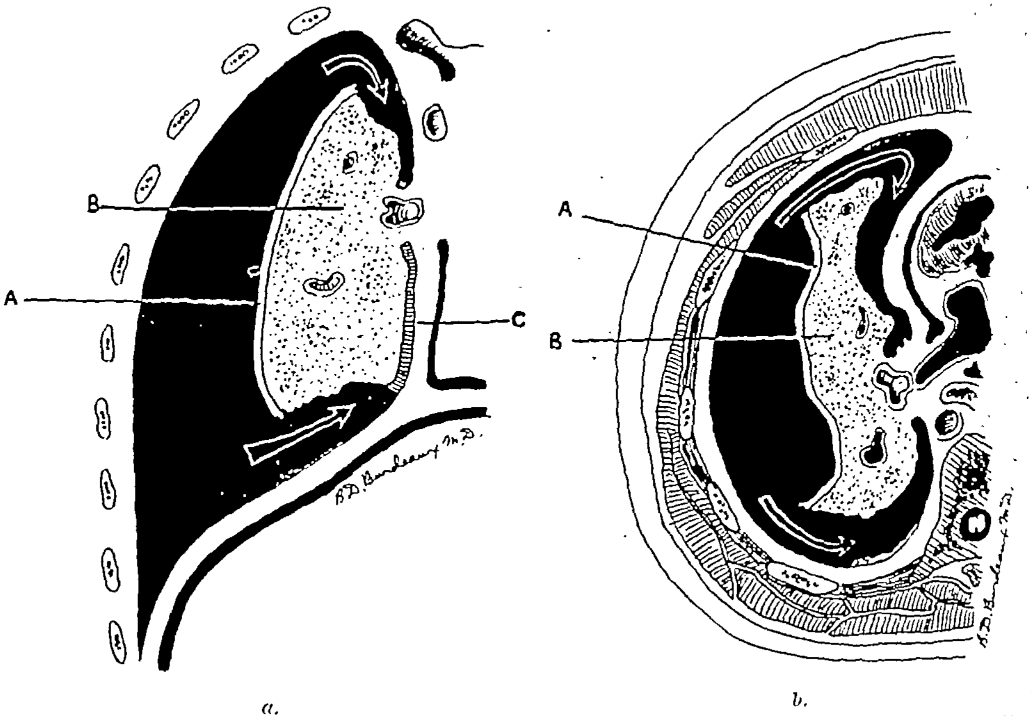
a. *b.*

Fig. 1.—Compression of the lung toward the mediastinum is illustrated in cross section (*a*) and coronal section (*b*). Pleural adhesions (*A*); peel (*B*); pleural space (*C*); compressed lung (*D*).

Granted that the lung is capable of expanding, a properly executed decortication is followed by a brilliant operative result in a high percentage of cases. Instances of partial successes and failures in important percentages are included, however, in the results of all who have had extensive experience with this procedure. Injury to the lung producing persistent alveolar leakage and delayed or incomplete expansion is the most important cause of such failures. Lung injury is especially likely to occur if blunt dissection is used to remove the peel of tuberculous patients having a postpneumothorax unexpandable lung. It is in this group that the technique to be described is especially advantageous.

OPERATIVE TECHNIQUE

With few exceptions,[8-11] the operative technique of Sampson and Burford[2] is currently being rather closely followed by others performing pulmonary decortication. This operation requires that the pleural contents, if present, be evacuated initially following which the peel is removed by blunt dissection. As the final step of the procedure, the lung is mobilized by dividing the pleural adhesions. Emphasis is placed on removal of the peel; and the matter of finding the proper plane of cleavage, control of bleeding, and repair of injuries of the lung is given detailed consideration. They discuss pleurolysis briefly and stress that it is an essential part of the procedure. Its importance as compared with removal of the peel is not considered.



a. *b.*

Fig. 2.—The step of pleurolysis is illustrated in coronal section (*a*) and cross section (*b*). The visceral peel has been divided at its periphery and the lung is being fully mobilized. In (*b*) all the adhesions have been divided and the lung is ready for inflation and decortication. This dissection is identical to that which would be required if pneumonectomy was to be performed.

The operation suggested here emphasizes the step of pleurolysis. It differs little from the preceding one except in the order of procedure and method of removal of the peel. The chest is opened using a thoracotomy appropriate for lower lobe lobectomy; this permits a better exposure of the diaphragmatic adhesions which are usually denser than those encountered elsewhere. Pleural contents, if present, are thoroughly evacuated. As the next step of the operation, the visceral peel is everywhere divided at its periphery. Complete pleurolysis is then performed, mobilizing the lung from the diaphragm, pericardium, chest wall, and mediastinum (Fig. 2). This has invariably proceeded readily with minimal bleeding and usually without injury to the lung, and can often be accomplished for the most part by manual dissection. When pleurolysis has been completed, the anesthetist is asked to inflate the lung. The degree of inflation that is possible at this point is usually surprisingly complete. Not infrequently, the lung can be inflated sufficiently almost to fill the pleural space with the peel still in place. The latter, moreover, shrinks considerably,[*] and appears to contract to approximately one-half its original size. The lung now being completely mobilized, the lower margin of the shrunken peel is elevated with clamps permitting the operator to develop a plane of cleavage between the peel and the lung in a vertical, rather than a horizontal plane. This enormously facilitates removal which is done using sharp dissection, alternating at times with the gauze covered finger as commonly practiced in isolating the sac of an inguinal hernia (Fig. 4). The laborious use of Küttner dissectors is entirely eliminated and the peel can usually be removed in a few minutes with almost no bleeding or injury to the lung. Performed in this manner, the removal of the peel actually becomes the least difficult part of the operation.

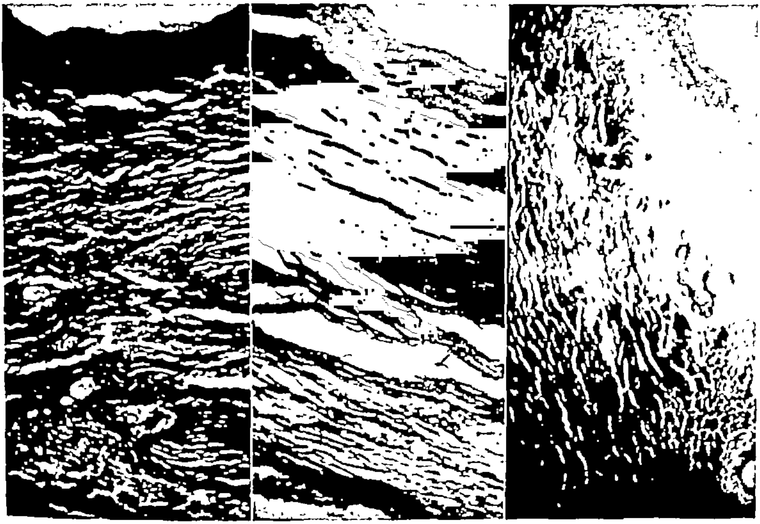


Fig. 3.—Photomicrographs of the peel of three patients is illustrated. The tissue was stained using the Verhoeff technique and was reported[†] as follows: "The sections disclose many of the individual fibers and masses of the collagenous tissue to stain black indicating presence of elastic tissue. Amounts of elastic tissue vary considerably from one area to another and from one section to another but in general it can be stated that the elastic tissue is quite abundant."

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[*] Shrinkage of the peel has occurred in patients having clotted hemothorax as well as in those having a postpneumothorax unexpandable lung. In the latter group, elastic tissue has been present in the peel in each instance (Fig. 3).

[†] Dr. Alexander A. Kosinski, Pathologist, C. S. Wilson Memorial Hospital.

The fissures of the lung are opened and the diaphragmatic adhesions are divided as is suggested in other publications. The removal of the parietal peel by dissection has not been done. An anterior and a posterior catheter connected with a subaqueous deflation system has been used to drain the pleural space. With one exception, which will be referred to later, minimal drainage and prompt re-expansion of the lung has followed permitting their withdrawal within forty-eight hours. In those having tuberculosis, streptomycin, 1 Gm. daily, has been administered for one week preoperatively and continued in similar dosage for two weeks after operation. All patients have received adequate doses of penicillin during the immediate postoperative period.

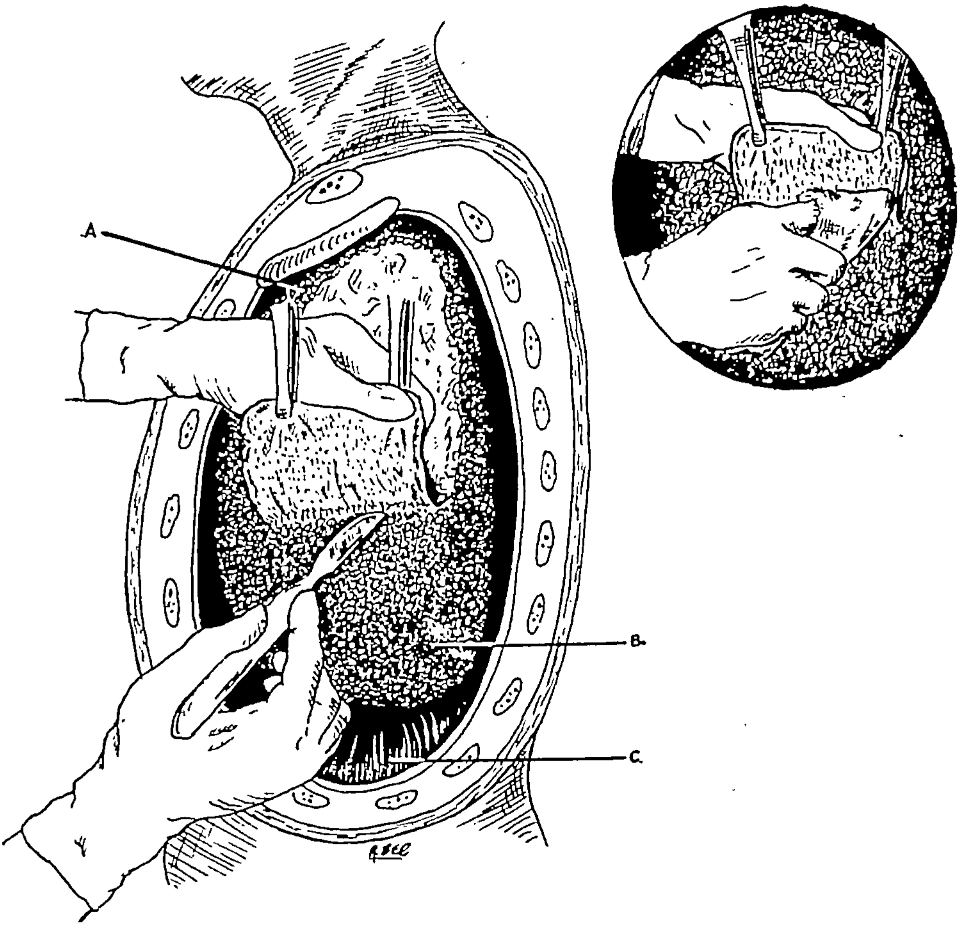


Fig. 4.—The manner in which the peel is elevated and removed is illustrated. Traction permits individual fine fibrous strands between the peel and the visceral pleura to be visualized and divided by sharp dissection. To avoid injury, the operator's attention should be focused on the lung and the knife should be applied to the peel. In this manner the lung is separated from the peel rather than the peel from the lung. The fibrous strands are avascular in instanecs of unexpandable artificial pneumothorax. The insert demonstrates dissection by the gauze covered finger which can be utilized when the peel separates readily.

In decortications performed on tuberculous patients having pneumothorax and an unexpandable lung, a factor of safety may be added by leaving the peel in place over the area which was originally the site of parenchymal disease.[18]

In such patients, additional filling of the pleural space by the lower lobe can often be obtained by dividing the pulmonary ligament.

The following case reports illustrate several features considered in the foregoing; in each instance, intratracheal ether-oxygen anesthesia was administered; the patient was placed in the lateral position and cotton suture material was used throughout.

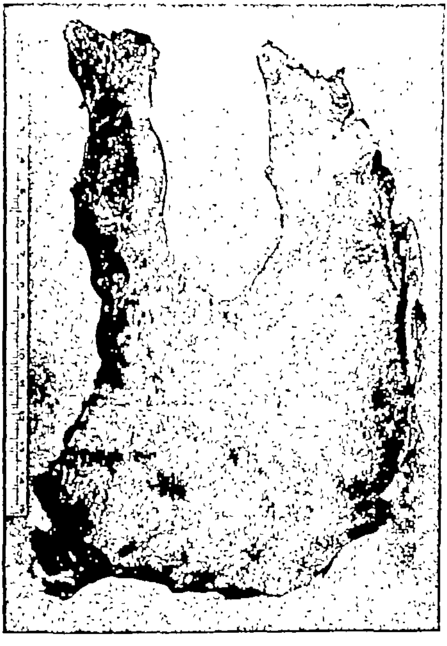
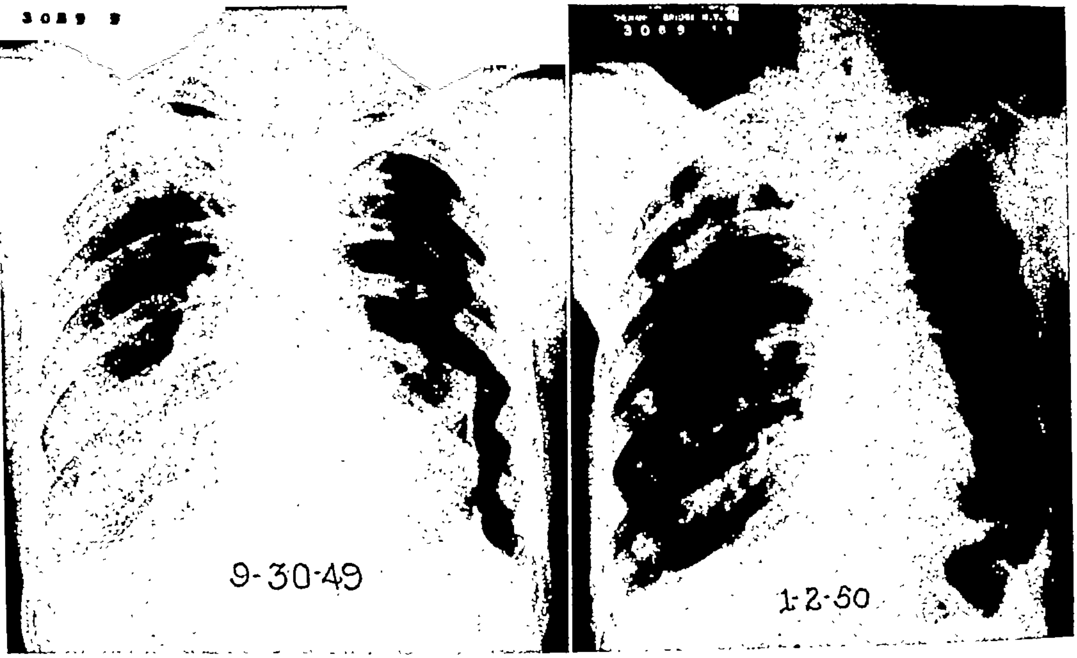


Fig. 5.—A photograph of the entire visceral peel removed from this patient is illustrated. The notch at the upper end is the area where a section of the peel was allowed to remain adherent to the lung. This comparatively small peel covered the entire lung which was compressed against the mediastinum.

Case 1.—C. G., a 23-year-old white man, had an artificial pneumothorax induced on Sept. 16, 1941, for caseous pneumonic tuberculosis of the upper lobe of the left lung. The patient also had disease in the upper lobe of the right lung without cavitation. Pleural adhesions were present and a closed pneumonolysis was done Nov. 28, 1941. Cavity closure and sputum conversion followed; he had pleural fluid on numerous occasions but never developed empyema. Attempts to expand the left lung were made during 1949, without success. Decortication by the technique described previously was performed on Oct. 24, 1949. After performing complete pleurolysis, inflation of the lung sufficient to obliterate more than one-half the pleural space was possible, with the shrunken visceral peel still in place. The latter was mobilized from below upward, and a portion of it was allowed to remain over the site of the disease in the left upper lobe (Fig. 5). The pulmonary ligament was divided; the fissures and diaphragmatic sinuses were opened, and the pleural space was drained with two catheters.

The postoperative course was uneventful; re-expansion of the lung was complete in thirty-six hours, at which time the catheters were removed. The wound healed by primary union and the patient was transferred back to another hospital* on the sixth postoperative day. Roentgenograms illustrating the preoperative status and the postoperative result are shown in Fig. 6.



a *b.*

Fig. 6. (Case 1).—The preoperative roentgenogram (*a*) and postoperative study (*b*) are illustrated.

CASE 2.—The following patient is of interest because the improvement which followed operation was due almost entirely to pleurolysis alone. This patient is an example of the type in which pulmonary fibrosis makes complete expansion impossible.

S. W., a 46-year-old man, originally had a large tuberculous cavity in the upper lobe of the right lung, which measured 5 cm. in diameter. Artificial pneumothorax was induced on April 1, 1940. Pleural adhesions were present, and a "difficult" pneumonolysis using enucleation technique was done on June 4, 1940. The cavity then developed tension characteristics, but nevertheless, closed six months later. Density persisted in the area formerly occupied by the cavity, and was believed to be due to inspissated secretions in the latter. The patient's sputum was converted; the pneumothorax was unexpandable. The patient stoutly refused thoracoplasty but accepted decortication. The operation was undertaken with some misgivings because of the size of the original cavity.

At operation, April 5, 1949, the peel was divided at its periphery and the lung mobilized. Re-expansion of the lower lobe was fairly good, and this was improved by division of the inferior pulmonary ligament. A large boggy area, roughly the size of the original cavity, could be palpated in the upper lobe. A similar area was present in the apical segment of the lower lobe. Because of these findings, it seemed unsafe to remove more than a narrow strip of the peel at its periphery, 2.5 cm. in width. A limited thoracoplasty would have been sufficient to obliterate the pleural space, but this was not done because permission for such a procedure had been refused. Following operation, considerable re-expansion has occurred but a small pneumothorax pocket persists. The patient's exercise tolerance has been greatly improved by the operation; he refuses additional surgery. His pre- and postoperative roentgenograms are illustrated in Fig. 7.

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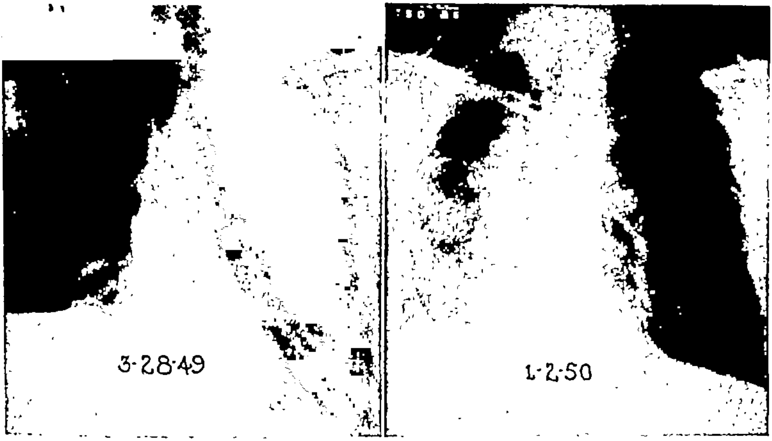
*Broome County Tuberculosis Hospital, Chenango Bridge, N. Y.



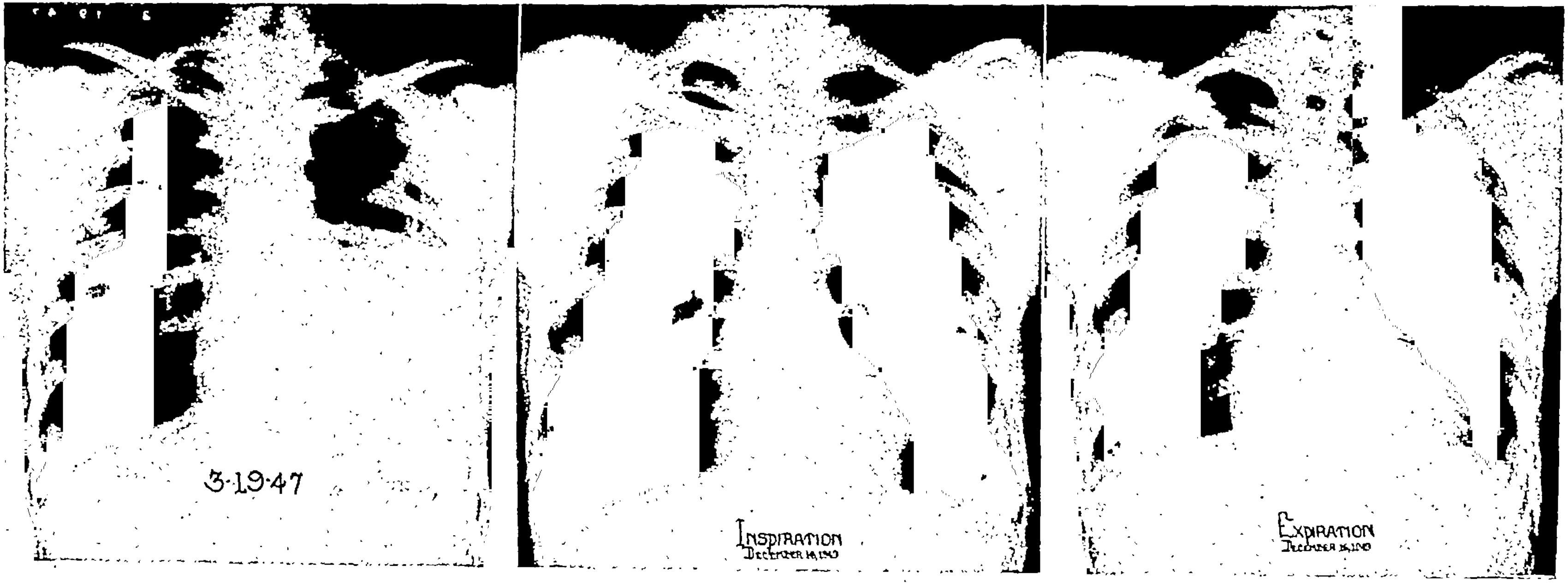
a. *b.*

Fig. 7 (Case 2).—The preoperative roentgenogram (*a*) and postoperative exposure (*b*) are illustrated. Mediastinal displacement has occurred following operation. This patient's exercise tolerance has been more than doubled since decortication.

CASE 3.—This patient is believed to be an example of so-called idiopathic spontaneous pneumothorax in which a torn vascular adhesion produced a simultaneous massive hemothorax. Elrod and Murphy[10] have reported a similar case operated upon in the same year. These authors believe that theirs was the first patient in this category to have been subjected to decortication.

R. B., a 14-year-old boy, developed sudden pain in the chest Feb. 25, 1947, while tobogganing. Dyspnea and shock followed rapidly. Upon admission to the hospital a short time later, signs of a massive left pleural effusion were present. Thoracentesis yielded pure blood and during the next three weeks repeated aspirations were done and 2,550 c.c. of blood were aspirated. During this period, blood transfusions totaling 2,000 c.c. were administered. When first seen by me, a small pneumothorax and signs of an organized hemothorax were present. The left lung and diaphragm were immobile.

Operation was performed April 1, 1947, in the manner previously described. At operation, the lung was immobile, and was collapsed approximately 50 per cent. After evacuating the pleural contents and dividing the pleural adhesions, it was possible to inflate the lung sufficiently almost to fill the pleural space. The peel was densely adherent over a 2 cm. area in the superior segment of the left lower lobe. This site was believed to be the source of the hemorrhage and the peel was not removed from this area. Elsewhere the peel separated readily, for the most part, by manual dissection. The parietal pleura was wiped with dry gauze, and the pulmonary fissures and diaphragmatic sinuses



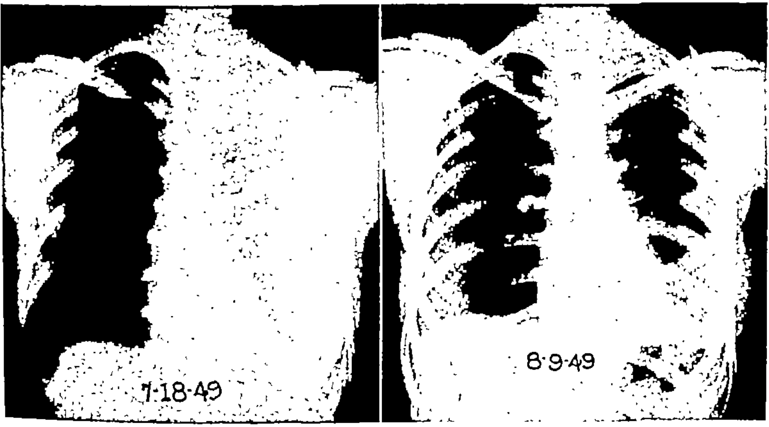
a. *b.* *c.*

Fig. 8 (Case 3).—The preoperative roentgenogram (*a*) and inspiration (*b*) and expiration (*c*) studies which were made two years and eight months after operation are illustrated.

were opened. The pleural space was drained with two catheters which were removed after forty-eight hours. Recovery was uneventful. Pre- and postoperative roentgenograms are illustrated in Fig. 8.

CASE 4.—The rapid re-expansion of the lung obtained in the following patient is of interest.

B. G., a 17-year-old white girl, had severe arterial hypertension, and underwent a two-stage thoracolumbar sympathectomy. During the second operation on the left side, an intercostal vein was opened, and the bleeding was arrested with Gelfoam. Severe intrapleural hemorrhage occurred postoperatively requiring numerous transfusions. Several aspirations were done by the surgeon but clotting occurred before the lung could be expanded. Decortication was done on July 28, 1949, five weeks after this operation. After preliminary pleurolysis, the peel was easily removed, using for the most part, blunt dissection. One small tear required a single cotton mattress suture. Drainage of the pleural space with two catheters was instituted, and the lung was fully expanded the following day. The patient made an uneventful recovery and was discharged from the hospital seven days after operation. Preoperative and postoperative roentgenograms of this patient are illustrated in Fig. 9.



a. b.

FIG. 9 (Case 4).—Preoperative roentgenogram (a) and postoperative study (b) are illustrated. The latter film was exposed on the twelfth postoperative day.

CASE 5.—This patient's lung was collapsed for over eight years. Although the parietal peel was not removed, excellent mobilization of the ribs and left hemidiaphragm has followed operation.

J. S., a 25-year-old white man, had a left artificial pneumothorax induced on Jan. 24, 1940. Caseous pneumonic tuberculosis was controlled, and sputum was converted. Pleural adhesions were present and these were divided by a closed pneumonolysis on March 19, 1940. Pleural fluid was subsequently present on numerous occasions but he never developed empyema. All efforts to re-expand the lung were ineffectual. Decortication was done as previously described in Case 1 on April 16, 1948. A portion of the peel was left in place over the site of the disease in the upper lobe. The lung was fully expanded in forty-eight

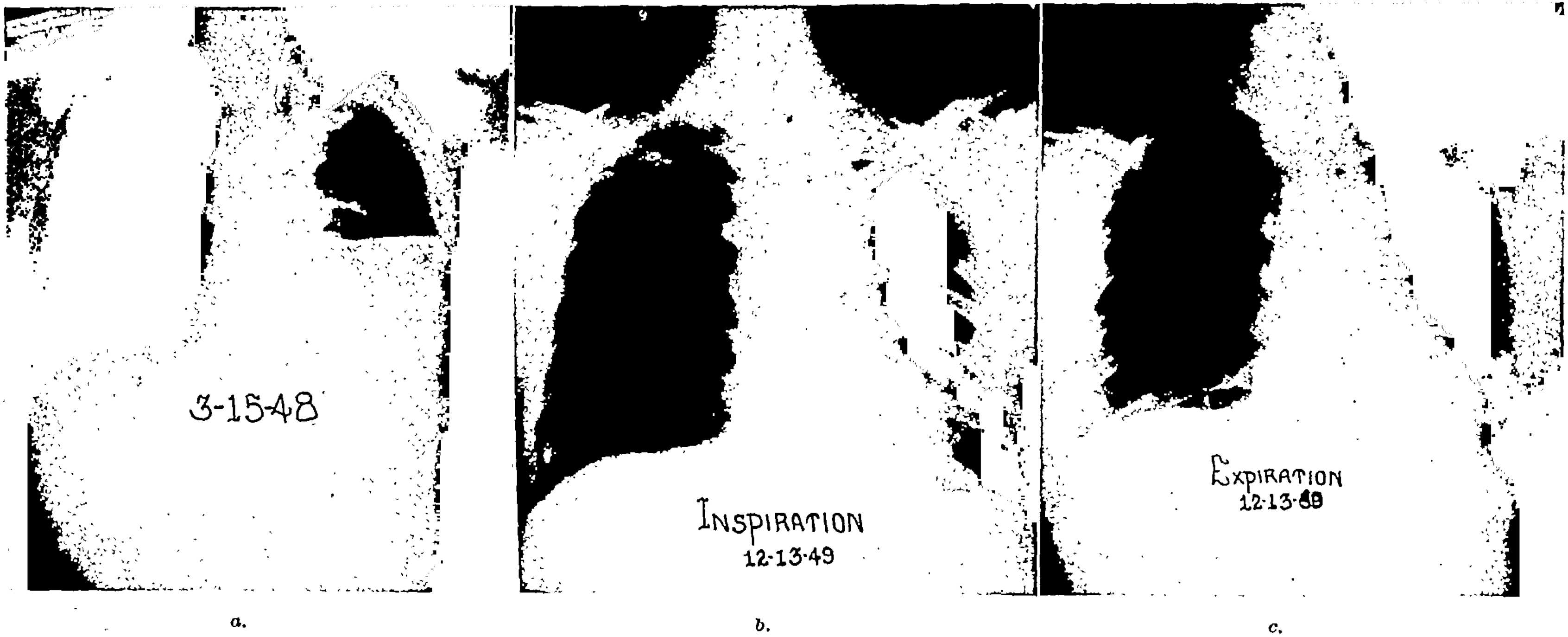


Fig. 10 (Case 5).—The preoperative roentgenogram (*a*) and inspiration (*b*) and expiration (*c*) studies made one year and nine months after operation are illustrated. Excellent mobilization of the ribs and diaphragm have followed operation. The parietal peel was not removed and the patient did not practice breathing exercises.

hours; convalescence was uneventful. The patient was transferred to another hospital six days after operation. At this writing he has been working for a period of eighteen months. Preoperative and postoperative roentgenograms are illustrated in Fig. 10.

CASE 6.—This patient had a pneumoperitoneum at the time of the operation. The procedure was well tolerated and prompt re-expansion of the lung occurred.

A. K., a 30-year-old married woman, developed pulmonary tuberculosis in April, 1944. A chest roentgenogram demonstrated an extensive bilateral exudative lesion with a cavity in the upper lobe of the left lung. Sputum was positive for acid-fast bacilli. An artificial pneumothorax was induced on the left side on May 14, 1944; adhesions were present and a closed pneumonolysis was done July 16, 1945. The patient's sputum was converted and she was discharged from the hospital Dec. 12, 1945. The patient was well until April, 1948; at this time she developed cough, fever, and weakness. Sputum was again positive and a roentgenogram demonstrated a cavity in the right lung. She was re-admitted to the hospital and streptomycin, 1 Gm. daily, was administered from April 8, 1948, until June 9, 1948. The infiltration in the right lung cleared, the cavity closed, and the patient was discharged from the hospital July 3, 1948. She remained well until July 26, 1949; at this time she developed fever and cough and a roentgenogram demonstrated a new cavity in the apical segment of the right lower lobe. Sputum was again positive. A pneumoperitoneum was induced July 28, 1949. The cavity closed promptly and sputum was converted within three months. During this period, attempts to re-expand the left lung were ineffectual. Decortication was performed Feb. 2, 1950. After division of the peel, the lung could be inflated sufficiently to fill almost completely the pleural space; it separated readily. Two small rents in the lung required closure with a 0000 cotton mattress suture. Drainage with two catheters was instituted as previously described. The lung was fully re-expanded the morning following operation. A small amount of drainage persisted and for this reason, the catheters were not removed until the second postoperative day. Convalescence was uneventful and the patient was transferred to another hospital six days after operation.

SUMMARY

In the foregoing, the factors that maintain pulmonary collapse in patients presenting indications for decortication are considered, and the importance of the role of pleural adhesions is emphasized. A change in the order of operative procedure is suggested, and a comparatively atraumatic and bloodless method of performing decortication is described. The procedure as outlined, is another application of an established surgical principle applicable to all dissections; namely, that adhesions which are least formidable should be divided initially, leaving those which are more difficult for the final step of the procedure.

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ADDENDUM

The operative technique described in this article has been used in decortication for tuberculous empyema; in this group it is believed that the parietal peel should be excised. A recent decortication for this disease was performed entirely without injury to the lung.

LOBAR AGENESIS OF THE LUNG

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AGENESIS of the lung is a rarely occurring congenital anomaly; however, lobar agenesis of one lung associated with an anatomic developmental abnormality of the bronchial tree is so exceptionally rare a manifestation that it is not specifically mentioned in the literature. During the past year the authors have had occasion to see two markedly similar proved cases of lobar agenesis of the lung and therefore present them as supplement to the data available on congenital lung malformation.

A search of the existing literature concerning cases which could represent a lobar agenesis of the lung yielded only two reports which might suggest such an anomaly if adequate proof had been available. Field[1] reported a case in which bronchography revealed a small left lung displaced posteriorly with a long main bronchus. There appeared to be no lingular branches. Confirmatory studies were not allowed by the parents of the patient. Ferguson and Neuhauser[2] reported a patient who was studied because of postulated atelectasis of the right middle and lower lobes. On bronchography a single bronchus was found on the right side which communicated only with the upper lobe. Although these two cases may have represented lobar agenesis of a lung, definitive anatomic proof is lacking.

A brief discussion of the embryology of the lung will serve to make more understandable the manner in which such an anomaly can occur. Two pulmonary anlagen may be differentiated: the epithelial and the mesenchymal. The earliest indication of the appearance of the epithelial anlage is the formation of a longitudinal groovelike evagination of the anterior wall of the foregut in the 3 mm. embryo. Fusion of the opposing edges of this evagination, termed the tracheoesophageal septum, begins at the caudal end and extends in a cranial direction, first splitting off the lung bud and then the trachea. When the embryo reaches the 4 to 5 mm. stage, the lung bud bifurcates; this represents the primordia of the main-stem bronchi. At the 7 mm. stage, the right-stem bronchus divides into three projections, and the left-stem bronchus divides into two projections. The bronchi grow by successive generations of monopodial branching into the thoracic cavities, pushing before them an investment of mesenchyma which adapts itself to the shape of the bronchial tree and fuses, ultimately, giving rise to the pulmonary lobes.[3]

A review of the literature pertinent to congenital pulmonary malformations reveals that a classification of agenesis of the lung was first made by Schneider[4] in 1912. Since that time the following definitions ordinarily have been employed as a basis for nomenclature:

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Agenesis of lung: where there is a complete absence of the lung and bronchi.

Aplasia of lung: where there is a rudimentary bronchus but no pulmonary alveolar tissue.

Hypoplasia of lung: where pulmonary tissue is underdeveloped in whole or in part of a lung.

In 1937, Hurwitz and Stephens[5] reviewed 34 cases of agenesis of the lung, and in 1944, DeWeese and Howard[6] increased this list to forty-four. Burger,[7] in 1947, reviewed an additional 10 cases which increased the list to fifty-four. Burger reported that 13 cases were to be found in the foreign literature, the details of these being as yet unobtainable. Since that time Field[1] has reported 3 cases, and Nesbit and associates[8] and Bowden[9] each have reported one. To date there are approximately 75 reported cases of agenesis of the lung.

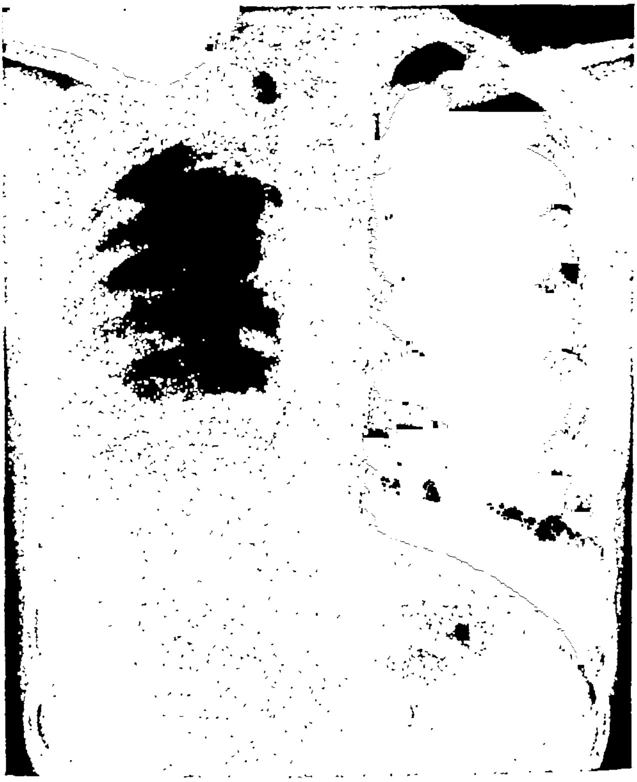

Fig. 1 (D. L. W.).—Roentgenogram showing deviation of the trachea to the right, elevation of the right diaphragm, dextrocardia, narrowing of the right intercostal spaces, and a diffuse density of the right hemithorax.

The majority of the cases reviewed in the preceding paragraph manifested severe degrees of agenesis, aplasia, or hypoplasia showing little or no functional lung tissue on the affected side. A variety of concomitant congenital anomalies were noted: cleft palate; agenesis of spleen, kidney and ureter; accessory thymus; esophageal atresia; tracheoesophageal fistula; diaphragmatic hernia; exencephaly; a variety of cardiovascular anomalies; hypoplasia of the face; dermoid of the eye; atresia ani, and incomplete lobulation of the remaining lung. It is of interest to note that of these cases, 14 showed a unilobular or an incompletely fissured remaining lung. In one instance three bronchi were recorded as supplying such a unilobular lung. It is unfortunate that no mention is made of the number of bronchi in the other cases reported. This is not in agreement with the generally accepted concepts of the embryologic development of bronchi and lobes.

In the following two case reports, the diagnosis of lobar agenesis of the lung was established in the first instance by exploratory thoracotomy and in the second by autopsy.

CASE REPORTS

CASE 1.—D. L. W., an 11-year-old white girl, was admitted to Childrens Hospital on Aug. 8, 1949, with the chief complaint of a "bad right lung." This patient had a persistent cough associated with many colds since the onset of whooping cough at the age of 5 years. During the recent winter months she had many upper respiratory infections associated with high fever and shortness of breath.

On physical examination the thorax was asymmetrical, there being a respiratory lag of the right hemithorax. The point of maximal cardiac impulse was shifted to the right of the sternum. There was relative dullness of the right chest, associated with diminished breath sounds.

A roentgenogram of the chest (Fig. 1) revealed an elevation of the peripheral portion of the right diaphragm. There was a diffuse density throughout the right lung field, associated with a marked shift of the mediastinum, including the heart, to the right. There appeared to be a herniation of the left lung across the anterior mediastinum. On fluoroscopy limitation of diaphragmatic movement on the right was noted.

A bronchogram (Fig. 2, *A* and *B*) revealed but one bronchus communicating with a single lobe on the right side. A bifid bronchial stump was noted projecting anterior to the visualized lobe. This was believed to represent an occlusion of the middle and lower lobe bronchi with compensatory enlargement of the upper lobe associated with a fibrothorax. The possibility of lobar agenesis of the lung was suggested. Because of increasing symptoms an exploratory thoracotomy was performed on Aug. 11, 1949.

On exploration of the right thoracic cavity, the pleural space was found to be completely obliterated by dense fibrous tissue. The right lung consisted of a single lobe covered by a fibrous membrane, which was peeled from the visceral pleura without difficulty. There was a blind bifid outpouching of the main bronchus anteriorly about 3 cm. distal to the carina (Fig. 3). This was considered to be the undeveloped primordium of the right upper and middle lobe bronchi. The right pulmonary artery was found to be 5 cm. in length. There was no branching of this artery until it entered the lower lobe, when it divided into the usual segmental branches. The lobe was supplied by a single vein occupying the anatomic position of the inferior pulmonary vein. The superior pulmonary vein was absent. On completion of the operation, the right lower lobe completely filled the cavity. The patient's postoperative course was uneventful and she was discharged on the sixth postoperative day.

CASE 2.—D. V. S., a 2-month-old white male infant, was admitted to Childrens Hospital on Feb. 11, 1948, with the chief complaint of "right lung obstruction and vomiting." This patient had had persistent vomiting since birth. On a previous admission to another hospital barium studies had ruled out the possibility of pyloric stenosis. X-ray studies of the chest had revealed atelectasis of the entire right lung, dextrocardia, and compensatory emphysema of the left lung. There was no history of aspiration of foreign bodies. No cyanosis was seen at any time. There was no history of familial disease or of congenital abnormalities.

On physical examination there was a respiratory lag of the right chest. The point of maximal cardiac impulse was located near the right nipple line. A soft apical systolic murmur was present. Breath sounds were short and diminished over the right lung field, and absent over the area of cardiac dullness. The left chest was hyperresonant.

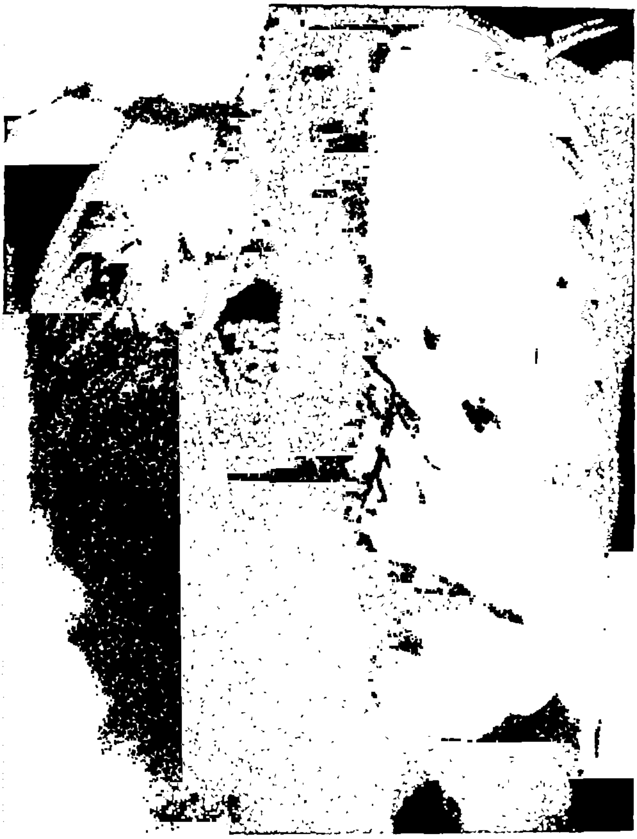

Fig. 2, *A* (D. L. W.).—Bronchogram revealing an anomalous right bronchial tree.

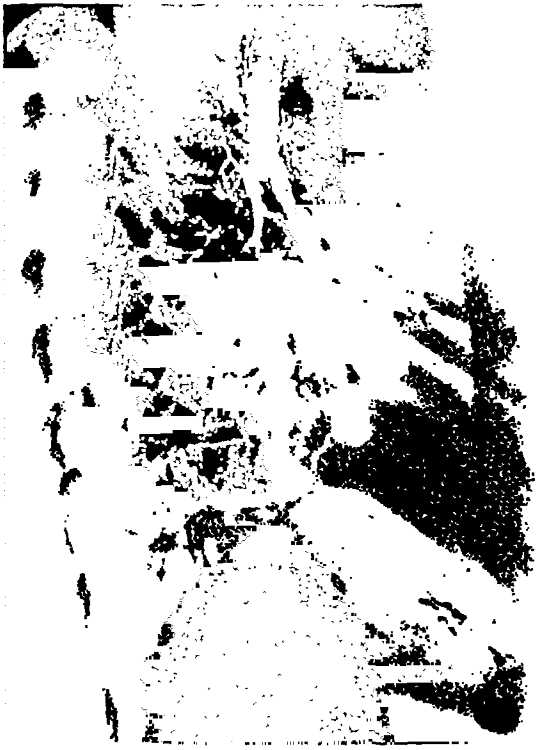

Fig. 2, *B* (D. L. W.).—Right lateral bronchogram which reveals undeveloped upper and middle lobe bronchi.

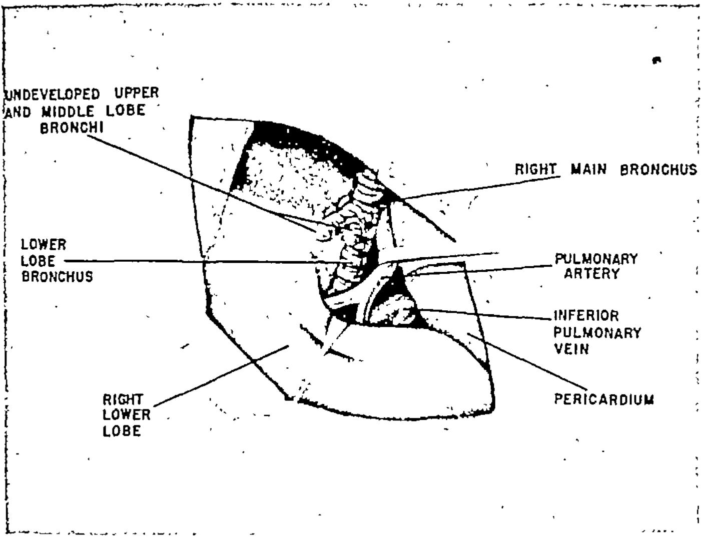

Fig. 3 (D. L. W.).—Illustration of the congenital anomalies and anatomic relationships as found during exploratory thoracotomy.

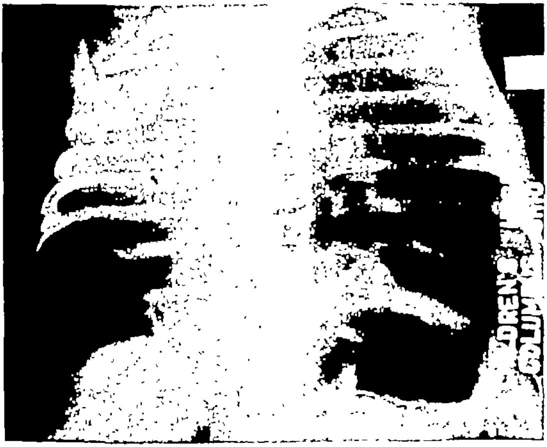

Fig. 4 (D. V. S.).—Roentgenogram showing right mediastinal shift, dextrocardia, and increased density of the right upper hemithorax.

Barium swallow and fluoroscopy showed the esophagus and trachea slightly deviated to the right. Chest roentgenograms revealed a mediastinal shift to the right (Fig. 4), with increased density of the upper three-fourths of the right lung field. The left lung was emphysematous. The heart was in the right hemithorax and its borders were indistinct and difficult to outline. On the basis of these studies it was concluded that the changes in the chest were due to massive atelectasis on the right; however, it was also suggested that agenesis of the lung should be considered. Bronchography and bronchoscopy were scheduled; however, the infant suddenly expired before these procedures could be performed.

Necropsy did not reveal the immediate cause of death. The pertinent findings were limited to the thoracic cavity. The right thoracic cavity showed diffuse fibrous adhesions between the pericardium and a single right lobe. The right middle and upper lobes were absent. The right-main bronchus communicated with the lower lobe without proximal branching. The left lung was emphysematous and herniated across the midline into the right hemithorax. The heart was located in the right chest. The final microscopic and anatomic diagnosis was lobar agenesis of the upper and middle lobes of the right lung.

DISCUSSION

Two similar cases of lobar agenesis of a lung are presented, parallels of which the authors have been unable to find recorded in the literature. In these two cases there was an agenesis of the right upper and middle lobes. One of these was proved by exploratory thoracotomy and the other by autopsy. Although Valle and Graham[10] were the first to report a case of agenesis of an entire lung proved by exploratory thoracotomy, we believe that this is the first case of lobar agenesis to be so proved. It appears that the abnormality of bronchial development as represented in these two reported cases must occur between the 5 mm. and 7 mm. stages of the human embryo.

SUMMARY

Two cases of lobar agenesis of the lung are reported, one of which was proved by exploratory thoracotomy, and the other by necropsy.

A discussion of the embryology and a review of the literature of lung agenesis have been presented.

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Original Communications

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEOESOPHAGEAL FISTULA

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Of all operable congenital deformities seen in the newborn infant, none is associated with more difficulties than congenital atresia of the esophagus with tracheoesophageal fistula. The infant is usually underweight and not infrequently premature. Other congenital deformities may be incompatible with life or may be of such a nature that multiple early operations are necessary. By the time a diagnosis is made many of these infants have pneumonia due to aspiration of saliva and liquids, or atelectasis as a result of occlusion of the bronchi. Such an infant, too weak to cough, and too feeble to cry, is a poor subject for a two to three hour anesthesia. The operative repair is long and tedious and the postoperative course is made stormy by all sorts of local and general complications. It is little wonder that the mortality continues to be rather appalling.

Leven[1] and Ladd,[2] in 1938, each saved the life of a child with tracheoesophageal fistula by tying off the distal end of the esophagus and exteriorizing the upper end, but to Haight and Towsley[3] goes the honor of being the first to close a tracheoesophageal fistula and to suture the ends of the esophagus together successfully. Since that time the continued work of Haight,[4] Ladd and Swenson,[5] Leven,[6] Gross and Scott,[7] Swenson,[8] Bigger,[9] and many others has added much to the successful care of these infants.

DIAGNOSIS

The diagnosis of tracheoesophageal fistula could so easily be made if at the time of delivery the possibility of such a deformity was considered in all newborn children who breathe poorly immediately after birth, have excessive

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From The Children's Memorial Hospital.

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mucus in the mouth and throat, and have cyanotic spells during the early hours after delivery. Unsuccessful attempts to introduce a catheter into the esophagus of such a child at once should arouse suspicion of congenital obstruction. Confirmation of the deformity is promptly established by introduction of a couple of cubic centimeters of Lipiodol through a catheter into the blind pouch and taking an x-ray picture. Ideally the diagnosis should be made before attempts at feeding result in regurgitation and aspiration.

Visualization of a blind upper end of the esophagus and the presence of air in the stomach or intestines makes a diagnosis of atresia of the esophagus *with* tracheoesophageal fistula (Fig. 1). However, if in the presence of atresia of the upper end of the esophagus, air is not seen in the gastrointestinal tract, a diagnosis is made of atresia of the esophagus *without* tracheoesophageal fistula. Occasionally the fistula between the distal esophagus and the trachea is so small that air does not pass through with ordinary respiration. In one such case a gastrostomy was done and feedings were begun. Pressure in the stomach forced milk upward through the fistula and caused fatal aspiration.

Fortunately, a congenital tracheoesophageal fistula is an uncommon deformity. Because it is uncommon the possibility of its existence is quite naturally overlooked.

ANALYSIS OF CASES

This review of 35 cases of atresia of the esophagus with and without tracheoesophageal fistula seen at the Children's Memorial Hospital during the past four years is presented, not as a proud display, but as a critical appraisal of the patient, its deformities, and their complications, of the methods of treatment, and of a possible simplification of the difficult technique of surgical repair.

The infant's weight at birth is of great prognostic significance. Nine of the 35 infants weighed less than 5 pounds on admission; 10 weighed between 5 and 6 pounds; 9 weighed between 6 and 7 pounds; and only 7 weighed 7 pounds or more. Furthermore, 4 of the infants were from two to six weeks premature. In 6 of the 9 infants weighing less than 5 pounds, the tracheoesophageal fistula was repaired and an end-to-end anastomosis of the esophagus performed. All died. Two of this group had extensive deformities incompatible with life and the ninth died following gastrostomy on the basis of a diagnosis of simple atresia of the esophagus. Later a fistula between the esophagus and trachea was demonstrated. The patient died after an attempt to close the esophagus transperitoneally.

Multiple deformities add to the hazard of operation. Besides the deformity of the esophagus one infant had a medulloblastoma of the cerebellum and two infants had subdural hematomas, all unsuspected, but found at post-mortem examination. Two infants had atresia of the rectum; one had bilateral extensive anomalies of the genitourinary tract; one had an interauricular septal defect, and one had a deformity of the ear and partial paralysis of the face.

The average age upon admission to the hospital was 3.4 days; the average age at operation was 4.1 days. The majority had pneumonia and/or atelectasis at the time of operation.

Three of the 35 infants had congenital atresia of the esophagus without tracheoesophageal fistula. One of these patients who had an antethoracic placement of the stomach followed by intrathoracic transplantation is reported in the following article in this issue of the JOURNAL. The balance, 32, had the most common type III deformity, that is, atresia of the upper end of the esophagus and a fistulous communication of the lower end of the esophagus with the trachea at or near the carina. Two were inoperable because of multiple deformities and died shortly after admission. One originally diagnosed as simple atresia of the esophagus proved later to have a small communication with the trachea.

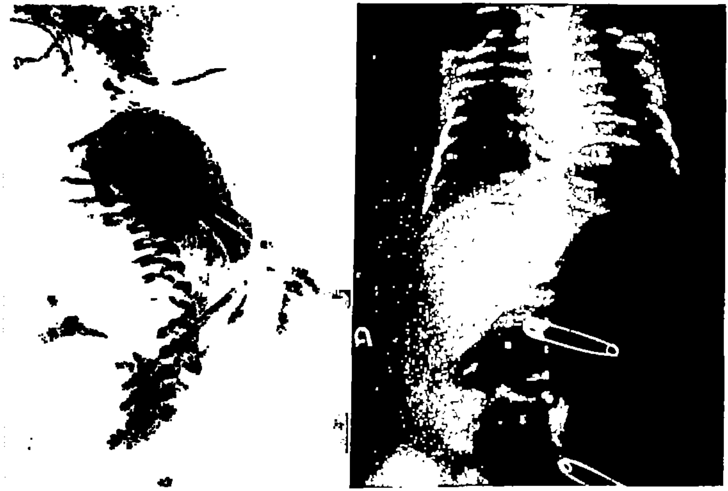

Fig. 1.—The blind upper end of the esophagus is filled with Lipiodol. Air in the stomach and intestine proves the presence of a tracheoesophageal communication.

Of the 29 patients with a classical type III deformity, primary anastomosis of the ends of the esophagus was done in 25. A preliminary gastrostomy followed by continuous suction as advised by Bigger was done in 3 patients to deflate the gastrointestinal tract and to allow time for treatment of the pneumonia. None survived this procedure. One child with associated congenital atresia of the rectum failed to survive a preliminary colostomy.

The 25 remaining patients with classical type III deformities are of primary interest. Closure of the tracheoesophageal fistula and reconstruction of the esophagus by end-to-end anastomosis was accomplished in all cases. Eleven of these patients survived the operation. One child died at 3 months of age because food would not go through the gastrointestinal tract. Exploratory laparotomy and later post-mortem examination failed to reveal the cause. Ten of the patients in this group are living and well.

PREOPERATIVE CARE

The preoperative care of these infants is demanding. Fluids are given with caution. If the child is dehydrated, sufficient 5 per cent glucose and small amounts of physiologic saline solution are given intravenously by needle or plastic tube in the saphenous vein at the ankle. While the average infant requires approximately 60 to 75 c.c. of fluid every twenty-four hours, per pound of body weight (15 c.c. per pound of this as saline solution), the infant with tracheoesophageal fistula is given about 40 to 50 c.c. as maintenance fluid requirement. Too much fluid to these patients, especially saline solution, may produce pulmonary edema.

On admission the child is immediately placed in oxygen. The pharynx is carefully aspirated with a soft rubber catheter about every half hour. Haight advised frequent turning of the infant and in case of atelectasis suggests placing the child on the opposite side with the head slightly lowered. Adequate doses of penicillin and streptomycin are immediately begun. Age and condition of the infant will determine the necessity for an immediate blood transfusion. During the operation approximately 10 c.c. of blood per pound of body weight is routinely given.

Bigger has made the excellent suggestion that gastrostomy be done before the tracheoesophageal fistula is attacked. Continuous suction on the gastrostomy tube not only deflates the gastrointestinal tract, but also prevents regurgitation of irritating gastric juice and bile into the bronchial tree. We have followed his advice in the treatment of 4 cases. The fact that 3 of the 4 died is due, not to any failure of the procedure, but to the extremely poor condition of the patients.

OPERATION

Anesthesia for these infants is a problem. We have used cyclopropane and oxygen administered through a tightly fitting face mask, or through an intratracheal tube. Recently we have been using open-mask ether. The last four patients operated upon have all had open-mask ether and all survived. No conclusions may be drawn from this sudden burst of good fortune. The small face mask is always handy for administration of pressure oxygen at a moment's notice. Likewise an intratracheal tube and laryngoscope are nearby for any emergency.

After the child is anesthetized, it is turned to the prone position with the right side slightly elevated and the right hand drawn upward (Fig. 2, *A*). Through a parascapular skin incision the rhomboid and trapezius muscles are cut and the scapula is retracted laterally. We resected subperiosteally segments of two, three, or four ribs until Leven suggested that instead we resect a long segment of one rib—the third or fourth. There is no doubt that resection of one rib is far superior to the removal of segments of a number of ribs. Exposure is better, there is less danger of tearing the pleura and the hazard of postoperative paradoxical movements of the chest is eliminated. The parietal pleura is carefully pressed away from the chest wall and vertebrae with a spatula and a tiny piece of gauze caught in the end of fine hemostat. The only place where there is real danger of injuring the pleura is during ligation of the azygos vein. Haight avoids this pitfall by not cutting the azygos vein but merely pushing it aside. If perchance, a hole is made in the pleura it is at once repaired if possible, otherwise covered with a pledget of gauze. The lung beneath is collapsed and retracted with a broad malleable retractor.

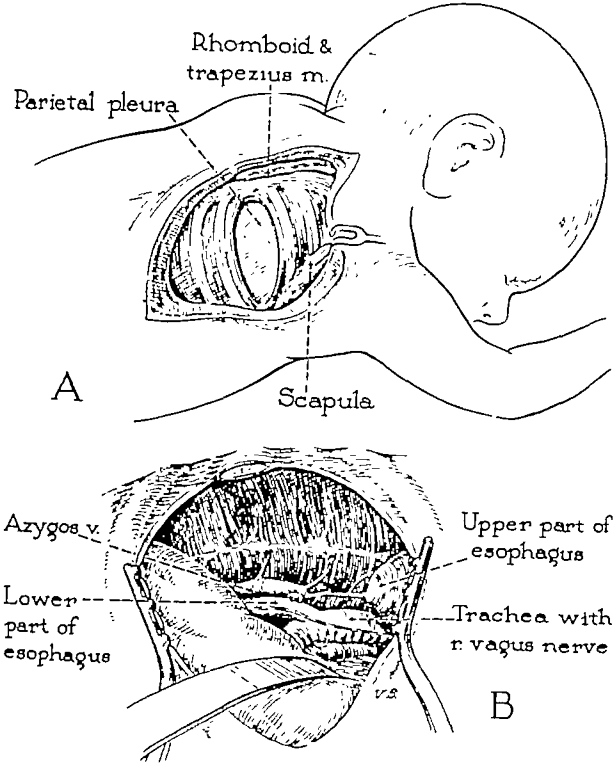

Fig. 2 *A* and *B*.—*A*, The fourth rib has been resected subperiosteally. *B*, The pathology is exposed.

The distal end of the esophagus is easily found and dissected free as far as necessary for proper handling. It is transfixed and tied with a silk suture near its attachment to the trachea. The esophagus is grasped with a fine-toothed clamp and cut near the transfixion suture. A few interrupted silk sutures are placed in the stump of the esophagus on the trachea (Fig. 2, *C*).

The upper end of the esophagus is caught at the very tip with an Allis forceps, drawn down, dissected from surrounding structures, and freed from its fibrous attachment to the trachea (Fig. 2, *C*). If there is the slightest difficulty in finding the upper end of the esophagus a catheter pushed down through the mouth will promptly identify it. A similar toothed clamp is now applied across the upper segment (angulated clamps are desirable because they allow more room for suture), and the small bit of muscularis caught in the Allis clamp is cut off. The muscularis is pushed up a bit and an opening to correspond to the size of the lumen of the lower segment is made in the mucosa (Fig. 2, *D*).

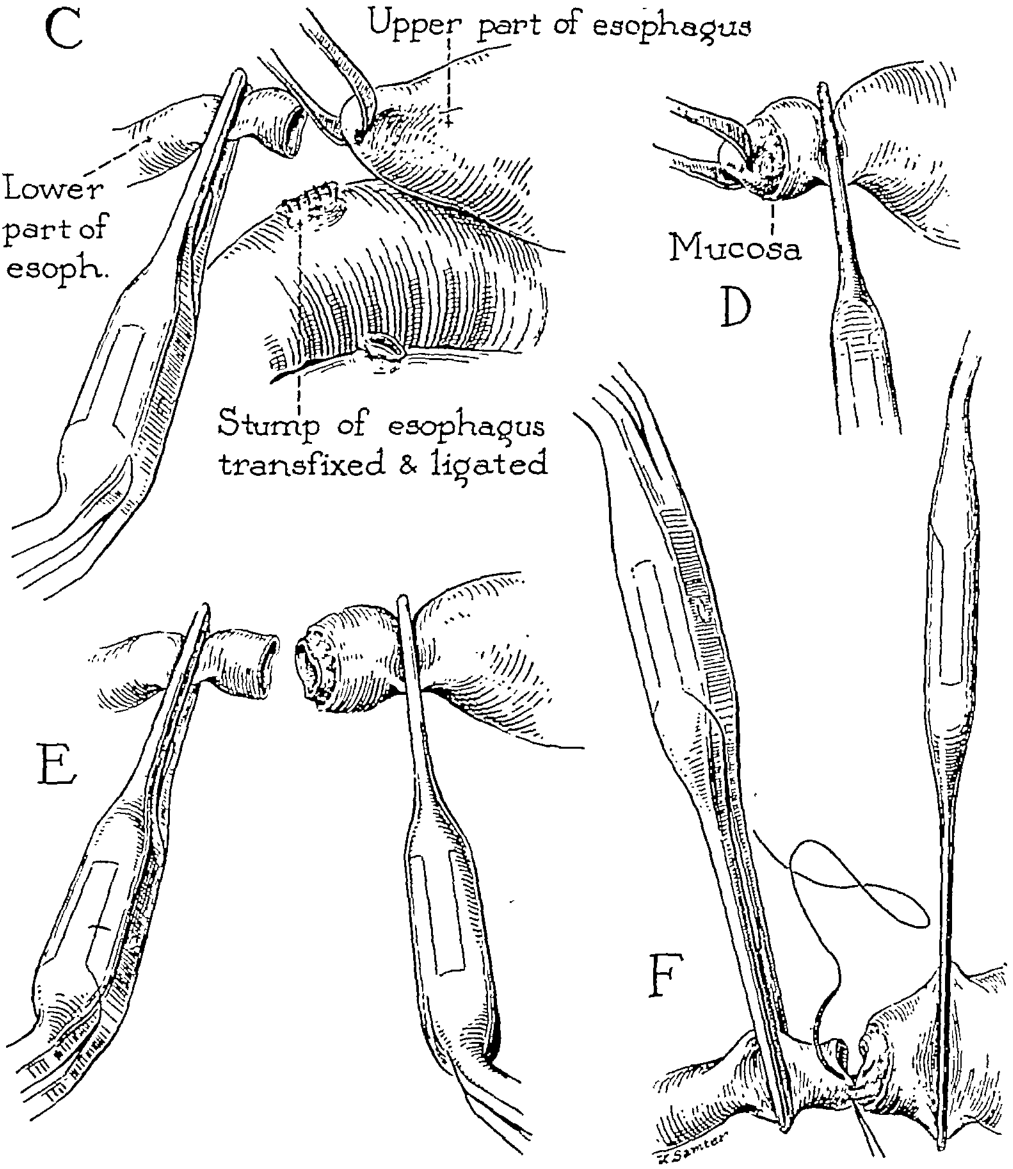

Fig. 2 *C* to *F*.—See text.

The ends of the esophagus are held together with the clamps. In the last six patients operated upon we have used the first models of the fine-toothed ductus clamps previously described.[10] These clamps are somewhat lighter than those routinely used at present for division of a patent ductus arteriosus. The teeth interdigitate slightly. Tearing of the muscularis occurred in one case because a heavier coarctation forceps was used. It is extremely important that the clamp be completely closed or it will slip and tear the esophageal wall. As the ends of the esophagus are being brought together most of the traction should be exerted on the upper end which is thick and strong. We have found the clamps superior to traction sutures which are likely to pull out and tear the esophagus. The telescoping technique of anastomosis advised by Haight is routinely used. With the clamps held straight up the posterior row of sutures between the mucosa of the upper segment and the entire thickness of the lower segment are placed (Fig. 2, *E* to *J*). Fine silk, 00000 Deknatel swaged on a small curved needle, has been used. We have recently used with satisfaction 000000 silk Deknatel on a smaller needle as advised by Haight. All the sutures are so placed that the knots are to the outside. After the posterior row of sutures has been placed the clamps are lowered and the anterior row is placed in a similar manner. The clamps are

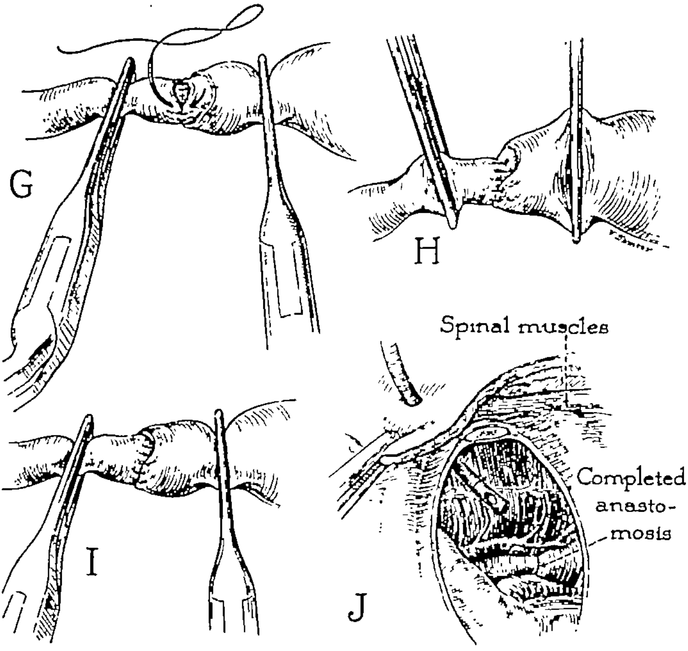

Fig. 2 *G, H, I,* and *J.*—*G, H,* and *I,* see text. *J,* The drainage tube is inserted through a small stab wound and is fixed to the fascia of the vertebrae.

again elevated and the muscularis is drawn down over the original line of suture and attached to the wall of the lower segment. Once more the clamps are lowered and the anastomosis is completed anteriorly in a similar manner.

Drainage of the mediastinum is absolutely necessary. Until Bigger published his paper on this subject in 1949, we routinely drained through the incision. Two patients died of collapse of the lung and tension pneumothorax outside of the pleura due to air aspirated through the wound presumably along the drainage material. Bigger's most valuable suggestion is that a drainage catheter be inserted through a separate small stab wound in an interspace below the incision near the edge of the vertebra (Fig. 2, *J*). The No. 10 or 12 French catheter with a couple of extra holes near the end is drawn through the stab wound into which it fits very tightly and is brought to lie near, but not against, the anastomosis. Pressure on the lung by the tip of the catheter can be avoided by throwing a fine catgut stitch around the catheter and suturing it to the fascia over the vertebra.

The lung is now expanded by adjusting the anesthetic mask to the child's face and making pressure on the anesthetic bag. After the lung has been completely expanded the chest is closed snugly by suturing the adjoining ribs together with a running suture of surgical gut. The wound is closed in layers with surgical gut and the skin with silk. While the anesthetist is making pressure on the anesthetic bag a clamp is applied to the drainage catheter to maintain expansion of the lung.

POSTOPERATIVE CARE

The infant is returned to an oxygenated crib. The drainage catheter is connected with a constant suction machine to remove any fluid, but above all to keep the lung expanded. To avoid excessive negative suction a water bottle with an escape tube, which allows only 10 cm. of water negative pressure, is connected in the suction system. The tube is left in the chest for at least ten days; suction is maintained until it is sure that the pleura is fixed.

Penicillin and streptomycin are continued. Fluids in the form of glucose, plasma, and occasionally blood, are given as necessary. Sodium chloride solution is given in very small amounts. The child is kept in oxygen a number of days. If mucus tends to collect in the throat, careful aspiration is done by a trained person who will not push the catheter down the recently sutured esophagus. Aspiration of the throat often stimulates a beneficial cough.

Until recently gastrostomy was routinely done forty-eight hours after repair of the esophagus. It is always done if leakage from the anastomosis is profuse. A gastrostomy in such cases is a necessary evil, the source of annoying and often disastrous complications. If there is no leakage, or if it is very slight, a gastrostomy now is not done. On about the third day the infant is given a few cubic centimeters of water every hour. The child is swallowing saliva anyway—it might as well swallow a little sterile water to help keep the esophagus clean. If all goes well the water is slowly replaced by a weak formula cautiously increased to a maintenance diet. In the presence of marked leakage, feeding by gastrostomy must be done by a slow continuous drip or the feedings will promptly flow out of the posterior wound.

Postoperative stricture of the esophagus at the point of anastomosis is expected if leakage has been profuse. To facilitate dilatation, it is desirable to have a string through the esophagus but to get it there may be difficult. The infant is given a fine thread by mouth and some formula to wash it down. If the thread does not come out of the back it is assumed that it is in the stomach. The stomach is filled with water and the gastrostomy tube is promptly removed. The thread floats out of the gastrostomy opening with the water—sometimes. A heavy string is then tied to the thread and drawn through the esophagus and the ends of the string are tied together. If the thread will not go down, a fine catheter is passed through the esophagus into the stomach under the fluoroscope. The catheter is fished out of the stomach and the string tied to its other end is drawn through the esophagus. From three to thirteen dilatations were necessary because of varying degrees of stricture in five children. The gastrostomy is kept open until it is demonstrated that no further dilatations are necessary. Dr. Paul Holinger and Dr. Albert Andrews, of the Endoscopic Department, prefer, when possible, to do retrograde dilatations of esophageal strictures with graduated bougies attached to a string and drawn through the esophagus.

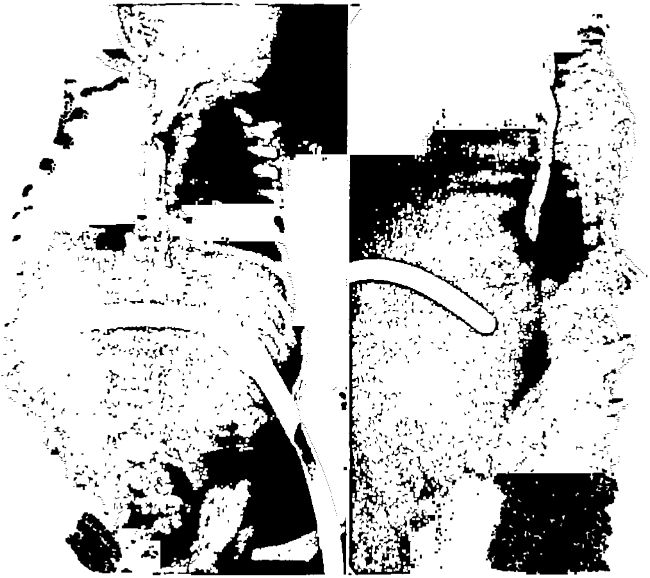

Fig. 3.—Anteroposterior and lateral roentgenographic views of an esophagus two weeks after anastomosis. No stricture developed.

Postoperative roentgenograms of the esophagus following a swallow of barium (Fig. 3) may appear discouraging but should not be interpreted too harshly. In spite of the deformity the child can usually swallow without difficulty. However, optimism should be controlled or a seemingly harmless deformity may suddenly terminate in total stricture very difficult to open.

SUMMARY

Thirty-five patients with congenital atresia of the esophagus with or without tracheoesophageal fistula are analyzed, not to justify, but explain the continued high mortality associated with surgical correction of these deformities. In 25 infants the fistula was closed and the ends of the esophagus were anastomosed. Eleven patients survived the operation and 10 are thriving and well from three months to three years following operation. Holding the ends of the esophagus together with fine-toothed clamps while the anastomosis is being performed appears advantageous in simplifying the technique of suture.

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(See discussion on page 701)

CONGENITAL ATRESIA OF THE ESOPHAGUS

Antethoracic Placement of the Stomach Followed by Intrathoracic Transplantation

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WHEN congenital atresia of the esophagus is associated with tracheo-esophageal fistula, *closure of the fistula and end-to-end anastomosis of the* segments of the esophagus are usually possible. (See preceding article in this issue of the JOURNAL.) However, in 3 infants who had congenital atresia of esophagus *without* communication with the trachea, the distal segment was too small and too short to be brought in contact with the upper segment. One of these children, 6 days old on admission, died two days after simple gastrostomy. An unsuccessful attempt was made in the second child to bring the widely separated blind ends of the esophagus together. Following gastrostomy and exteriorization of the upper end of the esophagus, the child did well for one year. Antethoracic placement of the stomach was then followed in a few hours by death from hyperpyrexia although the operation was simple technically. The third case, reported in detail, is of interest because of unanticipated difficulties corrected by a surgical procedure hitherto undescribed.

CASE REPORT

Marie H., aged 2 days, weighing 5 pounds and 3 ounces, was brought to the Children's Memorial Hospital in an oxygen cabinet, Dec. 12, 1947. At birth much fluid was aspirated from the throat before normal respiration was established. The puny, wrinkled infant was too feeble to cry. Thick mucus constantly collected about the baby's mouth. Injection of 2 c.c. of Lipiodol through a catheter into the upper end of the esophagus revealed atresia. Absence of air in the gastrointestinal tract indicated atresia without communication with the trachea (Fig. 1). The lungs were relatively clear. General physical examination revealed no other deformities. The child was kept in oxygen for twenty-four hours and given sufficient fluid in the form of 5 per cent glucose and saline solutions to meet physiologic requirements. The pharynx was aspirated each half hour.

On December 13, under closed mask cyclopropane anesthesia, through a right parascapular incision segments of the second to fifth ribs were resected subperiosteally. Extrapleural dissection of the mediastinal region revealed that the distal segment of the esophagus was *short and very small. In fact, at rest the segments of the esophagus were separated* by almost three inches and could not be brought together by traction. The chest wall was closed without drainage. During the operation 50 c.c. of whole blood were given by needle in the saphenous vein at the ankle.

The following day the resident correctly and frankly noted on the chart, "the child looks surprisingly good." She was kept in oxygen and frequent suction of the pharynx was continued. Weight fell to 4 pounds and 11 ounces.

On December 15, under general anesthesia a gastrostomy was done. The stomach was exposed through a muscle splitting incision in the right upper quadrant and a de Pezzer catheter inserted through a small incision in the stomach wall. The stomach in-

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From the Children's Memorial Hospital.

Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

cision was tightly closed about the catheter and the abdominal wound was closed. Small feedings were cautiously begun and built up to maintenance by December 18 when the child was 8 days old. Because transplantation of the stomach into the chest with anastomosis of the fundus to the upper end of the esophagus inside the chest was contemplated, exteriorization of the upper end of the esophagus at the neck was delayed. In retrospect this delay was unwise because atelectasis developed. Furthermore, in view of the respiratory difficulty this child had at 22 months of age when the stomach was placed in the chest, I do not believe it would have tolerated such a procedure during early infancy. Nursing care of the infant was a tremendous burden because of the necessity of frequent pharyngeal aspirations of mucus.

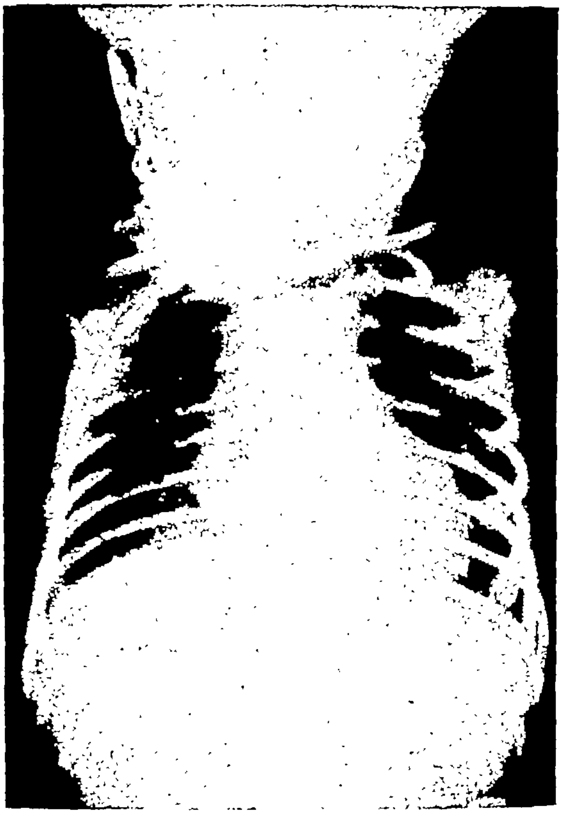

Fig. 1.—Absence of air in the gastrointestinal tract indicates atresia of the esophagus without tracheoesophageal fistula.

On December 31, the baby rather suddenly became cyanotic and showed dullness of the entire right chest. Roentgen examination revealed atelectasis. Prompt endoscopic aspiration of secretions in the bronchus improved the child's condition considerably. Repetition the following day was followed by return of breath sounds in the right chest and return of the heart to the left side.

On Jan. 16, 1948, the upper end of the esophagus was exteriorized above the left clavicle under cyclopropane anesthesia. The infant now improved rather promptly and was discharged from the hospital February 4, weighing 7 pounds and 7 ounces. Gastrostomy feedings were continued at home. On Sept. 28, 1948, at the age of 10 months the child, now weighing 15 pounds, 6 ounces, was readmitted to the hospital. About this time attention was called to an article by Rienhoff[1] describing antethoracic transplantation of the stomach and anastomosis of its fundus to the exteriorized cervical esophagus. Rienhoff, in a personal communication, vouched for the simplicity and nonshocking quality of this procedure. His predictions were substantiated.

On October 4, under ether anesthesia, a curved left rectus incision was made in the upper abdomen. The gastrostomy opening in the abdominal wall was freed and the gastrostomy closed with two layers of interrupted sutures placed parallel with the long axis of the stomach.

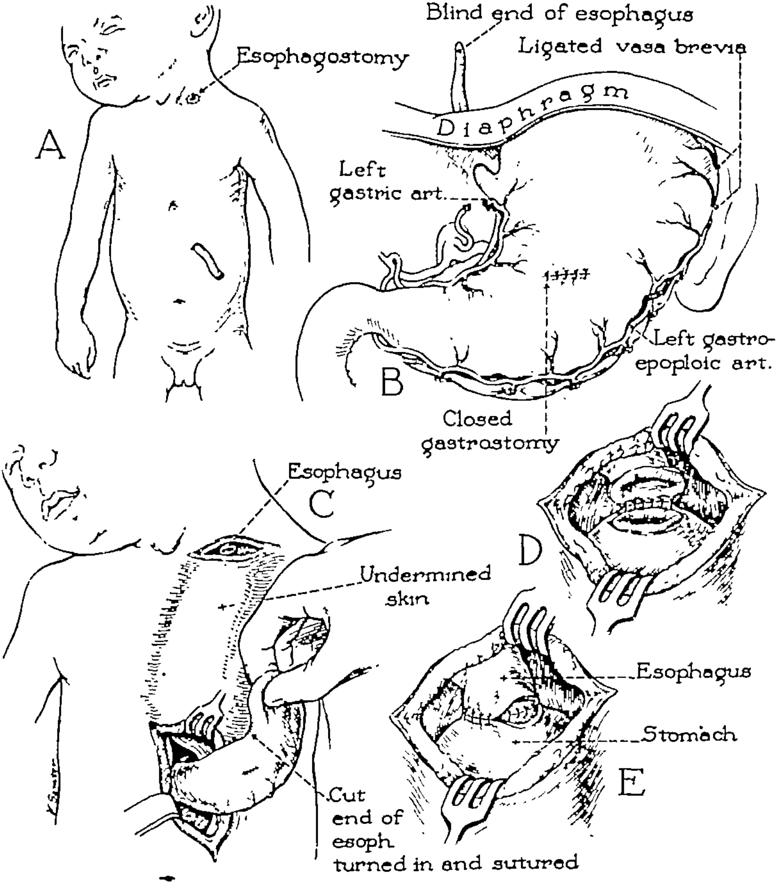

Fig. 2.—The stomach was freed, transplanted antethoracically, and its fundus anastomosed to the cervical stump of the esophagus.

The transverse colon was separated from the greater curvature of the stomach. The vasa brevia and the left gastric artery were doubly ligated and cut (Fig. 3). The lower segment of the esophagus was drawn out of the mediastinum with considerable difficulty but without accident. The esophageal stump was cut off at its point of entrance into the stomach and the opening closed with two rows of fine silk sutures parallel with the long axis of the stomach. The stomach was entirely freed.

A transverse incision was made above the left clavicle with the esophagostomy wound in the center of the incision. The end of the cervical esophagus was dissected free from the surrounding structures. The skin over the left part of the sternum and the anterior margin of the adjacent ribs was freed by blunt dissection from the xiphoid to the line of incision above the clavicle. The fundus of the stomach was grasped with an Allis forceps and drawn beneath the skin to the end of the cervical esophagus. It was interesting to note that the stomach could be drawn to this position without tension, in fact, it could easily have been drawn up another inch. An anastomosis between the cervical end of the esophagus and the fundus of the stomach was accomplished with two layers of fine interrupted silk sutures. It was gratifying to see free bleeding from the incision in the fundus preparatory to the anastomosis. The cervical and abdominal wounds were closed. Technically the operation was simple and free from shock.

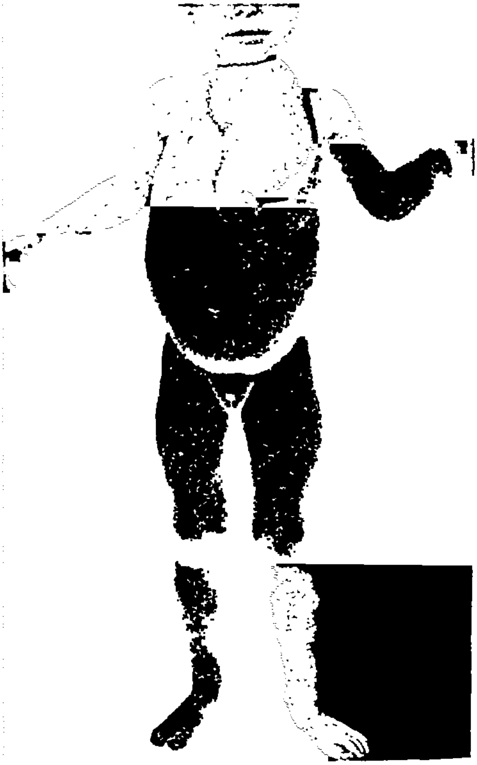

Fig. 3.—The subcutaneous stomach functioned well but was huge and unsightly.

The postoperative course was entirely uneventful except for a small stitch abscess at the outer angle of the neck wound. Four days after operation feeding was begun and by the tenth postoperative day a maintenance diet was being taken. A swallow of barium on the fourteenth day after operation went into and through the stomach without evidence of obstruction.

The child was dismissed from the hospital and in general progressed very well. Food was taken eagerly. The first few months after operation the subcutaneous stomach was not excessively large, but as months went by the stomach increased markedly in size (Fig. 3) although it functioned perfectly. After an ordinary meal the child's chin was literally buried in the fundus of its stomach. The parents were willing and eager that an attempt be made to correct the deformity.

Two methods of placing the stomach in the chest were considered; one, severing the esophagogastric anastomosis, freeing the stomach from its antethoracic position, drawing *it through the diaphragm to the apex of the chest, and reanastomosing it to the esophagus.* The idea of breaking down the anastomosis did not seem attractive. Consequently an alternative method not heretofore described was considered and tried in the post-mortem room. It appeared feasible.

On Sept. 28, 1949, the child, now 22 months old, was readmitted to the hospital and under intratracheal cyclopropane-oxygen anesthesia the following operation was performed. The stomach was thoroughly emptied. A cannula was placed in the saphenous vein at the ankle for administration of fluid and blood. A long skin incision was made from the left clavicle to a point midway between the xiphoid and the umbilicus. The stomach was easily separated from the skin and sternum. It had established no vascular communications with the surrounding tissue. The stomach was entirely freed from neck to the pylorus. The abdomen was opened sufficiently to expose the diaphragm.

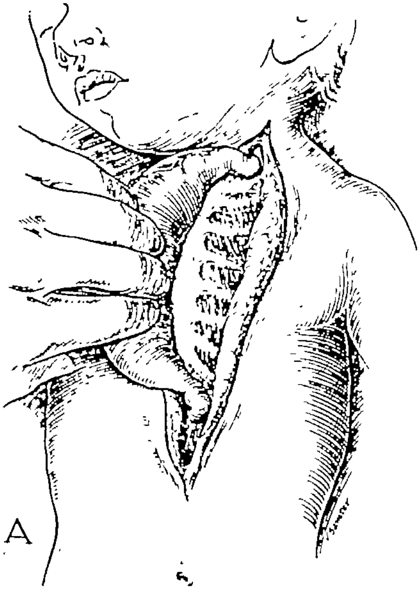

Fig. 4.—The stomach was freed and all the costal cartilages to the left of the sternum exposed.

Extensions of the fibers of the pectoralis major muscle were freed from the costal cartilages along the left edge of the sternum (Fig. 4). Beginning at the lower margin the costal cartilages, from the seventh to the second inclusive, were cut slightly lateral to the sternocostal junction. The intercostal arteries were tied as the ribs were cut. The pericardium was easily pushed away from the costal cartilages. As the upper ribs were cut the left pleural cavity was opened. The medial portion—approximately one-half—of the clavicle and a similar segment of the first rib were removed with the periosteum. The vessels beneath were pushed backward.

The diaphragm was now split straight back to the vertebrae. The ribs were retracted laterally, the stomach was placed in the left pleural cavity behind the lung and the heart, and fixed to the pleura in this position (Fig. 5). The diaphragm was repaired allowing sufficient room for stomach emptying. A de Pezzer catheter was drawn through the seventh interspace from the inside out for drainage. The costal cartilages were apposed and fixed, each with a through-and-through silk suture. The fascia of the pectoralis major muscle was drawn over the line of incision in the ribs and sutured to the sternum thereby giving an airtight closure of the chest. The lung was re-expanded and the catheter drain clamped. The abdominal portion of the wound was closed. The skin edges were coapted with a running silk suture. The esophagus lay easily in the depression made by resection of portions of the first rib and clavicle. The operation required two and one-half hours. A transfusion of 250 c.c. of whole blood was given during operation. The child was returned to her room in excellent condition and placed in oxygen. The drainage tube was attached to an under-water seal.

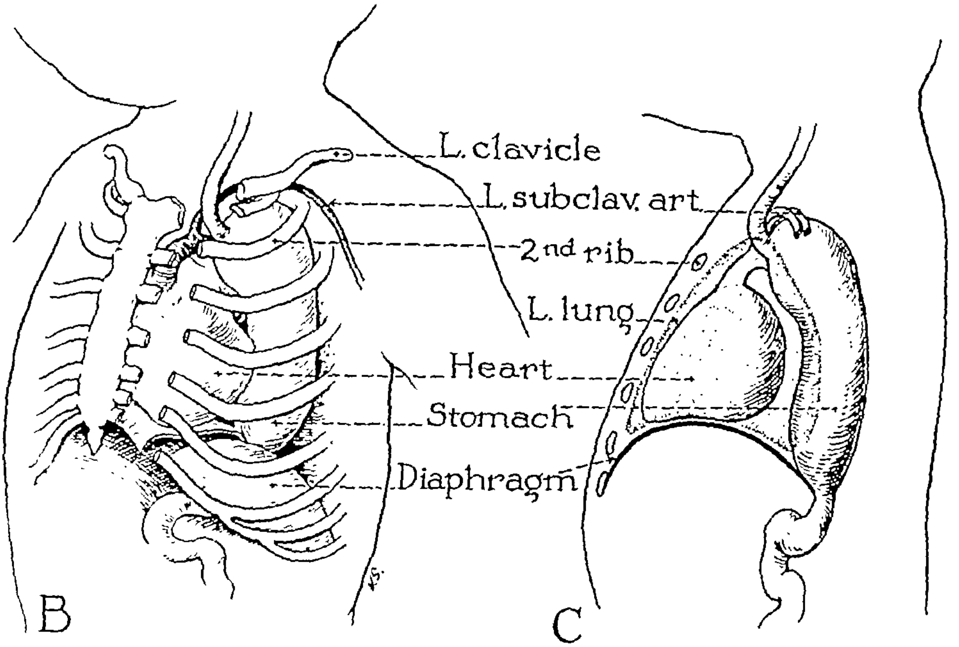

Fig. 5.—*B*, The costal cartilages were cut and segments of the first rib and clavicle were removed. The diaphragm was split.
C, The stomach was placed and fixed behind the lung.

For three days the child did very well and was started on a liquid diet including milk. The stomach became distended with air. Respirations became very rapid (70 to 80 per minute) and cyanosis was visible. For two days all food and fluids were refused. Her condition was precarious. A Levine tube was inserted transnasally into the stomach for feeding, but the child objected so strenuously that it was removed in twenty-four hours. Penicillin injections, intravenous fluids, and Levine tubes made the spirited child completely uncooperative. The mother, a very intelligent woman, was asked to come to the hospital to feed and care for the child. Promptly the child began to take fluids and food willingly and on the fourteenth day after operation was discharged in very good condition but exceedingly suspicious of every man in white (Fig. 6).

During the first month after operation she gained a pound in weight. Now, six months after the final operation, she is doing very well, eats four meals a day and plays vigorously. Respirations were somewhat rapid for a time but are now normal.

It is appropriate to mention gratefully the tremendous amount of time and care given this patient by the nursing and resident staff. Such children require almost constant nursing service. This child received approximately 600 injections of penicillin and streptomycin, 13,000,000 units of the former and 8 million units of the latter during the total hospitalization of 123 days. The residents administered 50 flasks of intravenous solutions, such as: blood, plasma, glucose, saline, and Amigen. Most of it was given intravenously. Every available vein in the legs, arms, and scalp was used to capacity.

DISCUSSION

Every effort should be and is being made by surgeons to bring together the ends of a congenitally atretic esophagus. At times because of wide separation of the segments, anastomosis is impossible and gastrostomy, plus exteriorization of the upper end of the esophagus, is necessary.

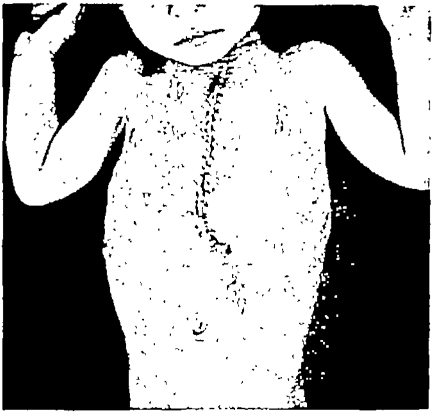

Fig. 6.—Photograph of child ten days after operation.

Various procedures have been devised to overcome the misfortune of a permanent gastrostomy. Ladd[2] had some brilliant successes and a number of failures in the construction of an antethoracic esophagus of skin tubes. Unfortunately, regurgitated gastric juice breaks down a skin tube esophagus and results in fistula formation. Swenson[3] in a number of cases constructed an esophagus of jejunum which he placed antethoracically beneath the skin and anastomosed to the exteriorized cervical esophagus. In this procedure, since the stomach is by-passed, irritating gastric juices cannot reflux and produce fistulas. He had difficulty in some cases in bringing the jejunum to the esophagus and had to insert a short skin tube. Harrison[4] has brilliantly accomplished the construction of an *intrathoracic* esophagus in two cases from a segment of jejunum. This operation, done in three stages, has the decided advantage of avoiding the cosmetic defect of any type of subcutaneous esophagus. Anastomosis of the distal end of the transplanted jejunum to the stomach, as done by Harrison, is also desirable. Sweet[5] successfully restored continuity of the alimentary canal by transplanting the stomach of a 21-month-old child into the chest and anastomosing the fundus to the cervical esophagus. Considering the distressing and alarming dyspnea our patient at age 22 months had for a few days after intrathoracic placement of the stomach, it is doubtful whether such an operation should be done during early infancy when encroachment on respiratory space is poorly tolerated. All methods devised for restoration of a normal food passage are worthy of consideration and development. Failures and a high operative mortality should not discourage surgeons from making strenuous efforts to relieve a child of the distressing burden of a permanent gastrostomy.

CONCLUSION

Although the case of this child terminated happily, antethoracic transplantation of the stomach is not advised.

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(See discussion on page 701)

RECONSTRUCTION OF ESOPHAGUS

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Reconstruction of the entire esophagus with a transthoracic jejunal transplant was first reported by Dr. Albert Harrison[1] at the meeting of this Association in Quebec in June, 1948. His work was based in turn upon that of Rienhoff,[2] Yudin,[3] Herzen,[4] and Roux.[5] Rienhoff was the first to transplant the jejunum within the thorax and has described fully the historical development of the operation in his article.[2]

Harrison performed his operation in three stages. At the first stage a tube of jejunum was prepared with one arcade of blood supply, isolated, brought up through the transverse mesocolon, and the distal end anastomosed to the stomach. Jejunal continuity was restored by end-to-end anastomosis. Two weeks later the left chest and diaphragm were opened and the esophagus divided at the cardia, freed, and brought out through an incision in the neck along with the proximal end of the jejunal tube. Finally, two weeks later the esophagojejunal anastomosis was made in the neck.

While listening to Dr. Harrison's excellent presentation, one was impressed with the magnitude of his procedure. The second stage of the operation seemed relatively shocking and freeing the transplanted loop of jejunum without injuring the blood supply appeared difficult. This feeling was confirmed during the discussion when Dr. Sweet stated that "the operation is not an easy thing to accomplish."[6]

A few weeks later, with these thoughts still in mind, a thymectomy was performed for myasthenia gravis. The ease and safety of dissection in the anterior *mediastinum suggested a new location for the transplanted jejunum.* It appeared that a relatively short tunnel could be made in the anterior mediastinum, safely, and, with a minimum of shock. A one-stage operation might be possible and many difficulties avoided.

Dissection on cadavers confirmed many of these suppositions. It was found that the internal mammary arteries were protected by the transverse thoracic muscles and the insertion of the sternothyroids (Fig. 1). If the anterior mediastinum is approached from above and below exactly in the midline, the dissecting fingers can press close to the under surface of the sternum and costal cartilages and, remaining safely in the plane of the endothoracic fascia, push back the parietal pericardium and parietal pleura to form a tunnel from abdomen to neck large enough to admit a hand (Fig. 2).

As in Dr. Harrison's cases, reconstruction of the entire esophagus was desired most often for lye strictures, but one hesitated to attempt an untried

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Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

procedure on these patients. So it was first used as a palliative for inoperable carcinoma of the esophagus.

The technique changed as complications were encountered. Rienhoff's method of preparing an antiperistaltic tube of jejunum (Fig. 3) was used at first, but later abandoned reluctantly as the importance of the direction of

FIGURE 1

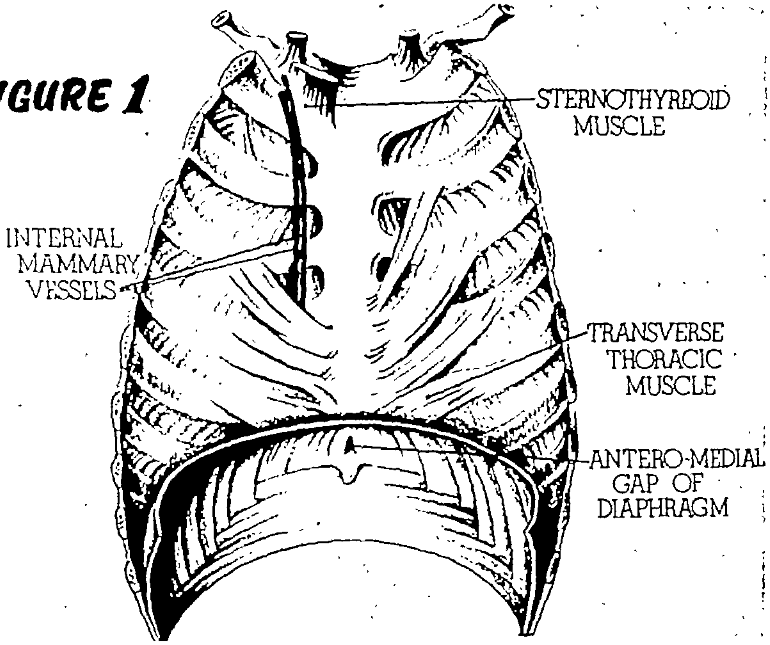


Fig. 1.—Anatomy of anterior chest wall viewed from behind.

FIGURE 2

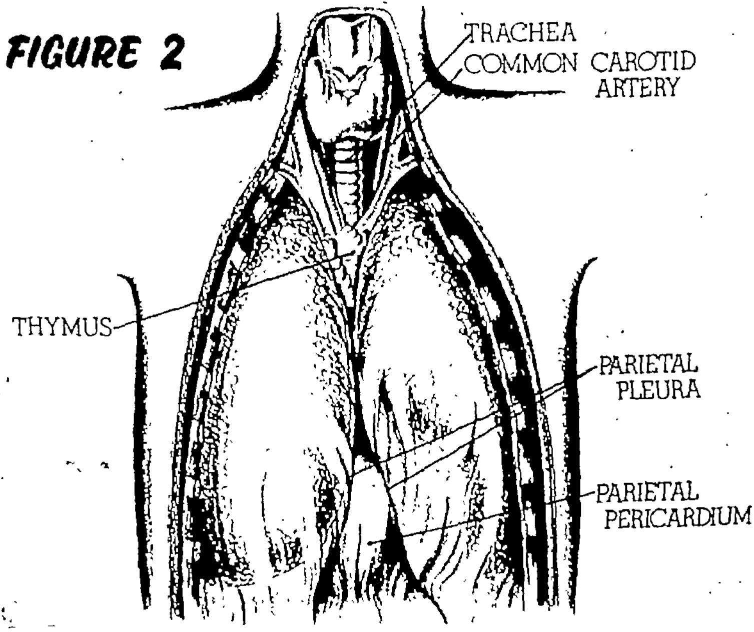


Fig. 2.—Anatomy of anterior mediastinum, the anterior chest wall having been removed.

peristalsis became evident. Our present technique as formed by the pressure of experience is as follows.

PRESENT TECHNIQUE

The intra-abdominal part of the procedure is best carried out through a left paramedian rectus-displacing incision extending from one inch above the xiphi-sternal junction to one inch below the umbilicus. This incision allows easy retraction to the right

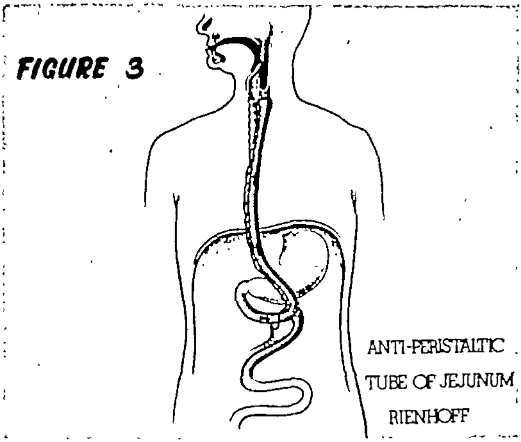


Fig. 3.

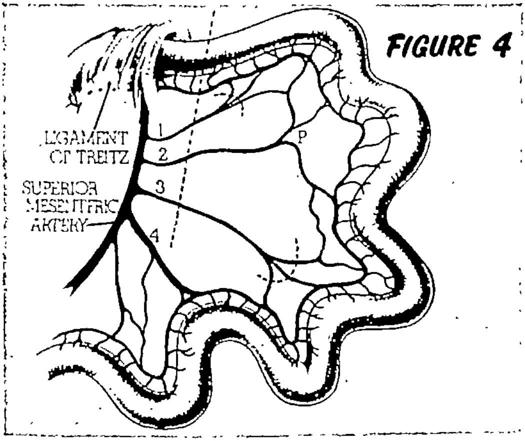


Fig 4.—Straight dotted line indicates sites for division of jejunum and vessels in preparing an isoperistaltic tube. Curved dotted lines indicates sites for division of secondary branches if additional length is required. The letter *P* indicates the preservation of secondary branches when the arcade appears dangerously thin.

of the ligamentum teres of the liver and, during the closure of the wound, facilitates the closing of the peritoneum around the jejunum as the latter passes from the peritoneal cavity to the anterior mediastinum.

The jejunum is brought out of the abdominal cavity, spread fan-wise on warm moist towels, and the distribution of the superior mesenteric artery studied (Fig. 4). The relative sizes of the first four or five branches should be noted. If the fourth or fifth branch is a large one, it means that the first three or four can be severed without jeopardizing the blood supply of the bowel, because the retrograde flow through the arterial arcade close to the intestine will be adequate. This can be tested by simultaneous digital compression of the vessels chosen for division. The jejunum may then be divided near the ligament of Treitz and therefore permit the distal end to be anastomosed to the esophagus in an isoperistaltic manner (Fig. 5).

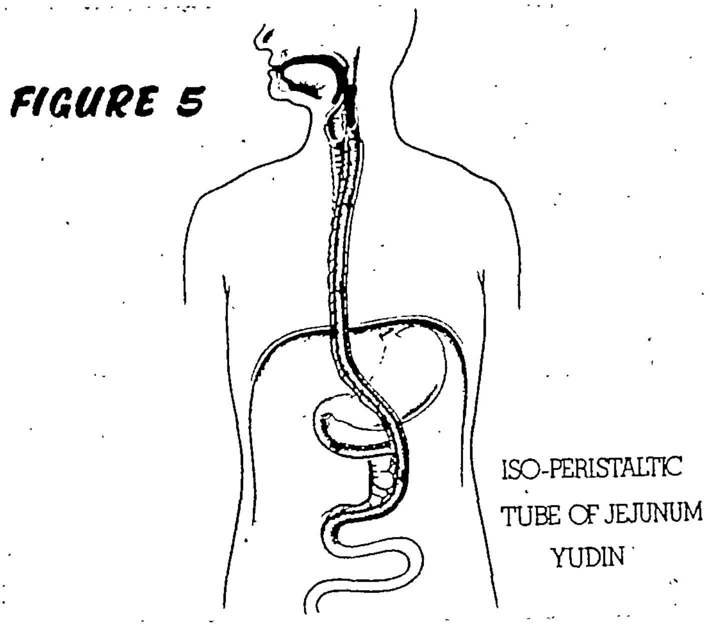


Fig. 5.

The distance from the thyroid cartilage to the region of the ligament of Treitz should be measured with a piece of tape which is kept for frequent use while preparing the jejunum. The marked tape is laid along the line of the vascular arcade of the mesentery to get an approximate idea of the length of jejunum required. The peritoneum of both sides of the mesentery of this length of jejunum is then totally removed from the root of the mesentery outward to the edge of the jejunum. This is facilitated and shock is reduced by injecting 0.5 per cent Novocain subperitoneally on both sides of the mesentery. Great care is taken to avoid even minor hemorrhage, lest an important anastomosing vessel might have to be tied. All nerve fibers running in the mesentery are divided, for they greatly limit the eventual straightening of the length of jejunum. The branches of the superior mesenteric artery and their accompanying veins are then individually ligated, close to the main artery, beginning with the first branch and proceeding distally until the required length of jejunum has been obtained. We have not had to divide more than four branches.

The jejunum is then divided about two inches distal to the ligament of Treitz, leaving just sufficient beyond the ligament to allow an end-to-side anastomosis to be made later. A clamp is left on the proximal end, but the distal end is tied and transfixed with heavy silk and the ligature left about eighteen inches long, so that subsequently it can be passed up through the anterior mediastinum. The portion of jejunum to be transposed is now straightened out and any additional nerves or other tissue limiting this procedure are divided. We have found it possible to obtain greater length by ensuring that all peritoneum has been completely removed right up to the bowel. If secondary branches of the divided arteries limit the straightening of the jejunum, they may be divided if it is demonstrated that additional adequate anastomoses exist between them (Fig. 4). Veins must not be ligated any more freely than arteries, for venous drainage is just as important as arterial supply.

Having prepared the jejunum for its transposition, considerable time can be saved by continuing the operation as two surgical teams. One team completes the abdominal part of the procedure, while the other team exposes the esophagus in the neck and does the esophagojejunostomy.

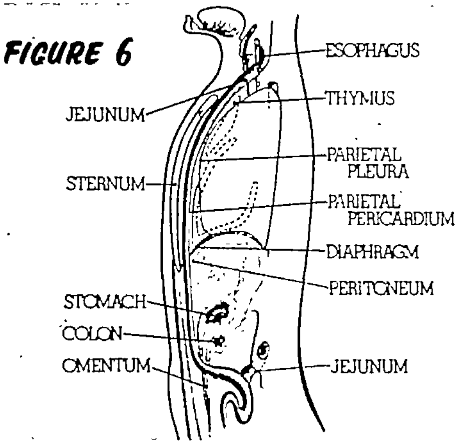


Fig. 6.—Sagittal section illustrating location of jejunal transplant in anterior mediastinum.

From the abdomen, the anterior mediastinum is entered (Fig. 6) through the anteromedial gap of the diaphragm, by blunt dissection upward and to either side, close to the deep surface of the xiphoid process and costal cartilages. If the xiphoid process is long, it can be removed. The diaphragm is then separated from the costal margin by blunt dissection for two inches on both sides of the midline. This allows the surgeon's entire hand to enter the anterior mediastinum. Blunt dissection with the fingers is gently carried upward anterior to the pericardial sac, carefully pushing both pleural reflections laterally. No troublesome hemorrhage has been encountered during this procedure. Gradually the hand is worked upward until it meets the fingers of the other surgeon working downward from the neck.

The cervical incision is made along the anterior border of the left sternomastoid muscle well down over the episternal notch. The left side is chosen as the lower cervical esophagus deviates slightly to the left. The deep fascia is then opened down into the suprasternal space, the left strap muscles divided, and the esophagus approached between the trachea and the carotid sheath (Fig. 7). The recurrent laryngeal nerve is then identified and protected and the cervical esophagus freed from the trachea and cervical spine and drawn up into the wound. The esophagus is clamped with slotted forceps below, narrow forceps above, divided, and the stumps carbolized. The distal stump is then sutured with continuous chromic catgut through the slotted forceps and invaginated with an additional layer of interrupted black silk.

The anterior mediastinum is then tunnelled with the fingers from above keeping close to the sternum and separating the inner part of the insertion of the sternothyroid muscle. Space should be made to admit three fingers.

The long ends of the heavy silk tie on the proximal end of the jejunum to be transposed are now passed up through the anterior mediastinum and the jejunum very carefully drawn upward. Great care is taken not actually to pull on the narrow mesentery of the bowel for fear of injuring an artery or vein. The jejunum is pushed up through the mediastinum rather than pulled, and the silk ligature used as a guiding string. An attempt is made to lay the jejunum on its side and to avoid kinks, for the length of the bowel is always greater than the length of the mesentery.

FIGURE 7

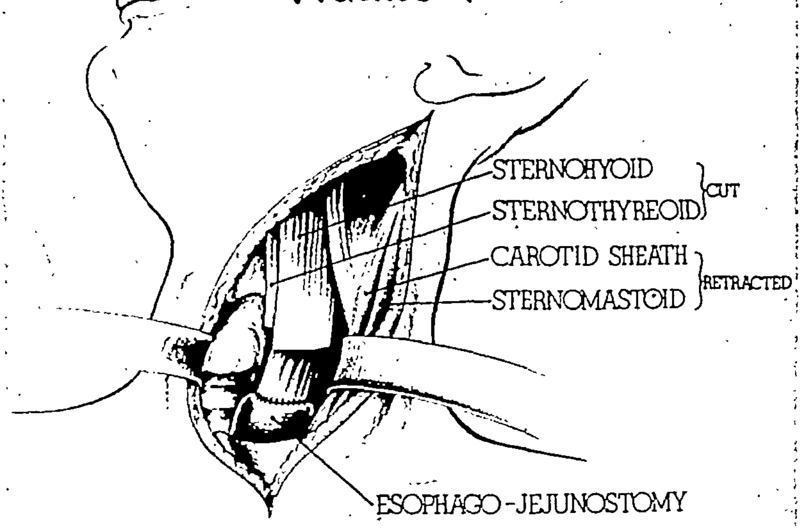


Fig. 7.—Jejunum anastomosed to esophagus in the neck.

Excess length of jejunum is excised and the upper esophagus divided above the narrow clamp. The esophagus and jejunum are then anastomosed meticulously with two layers of interrupted invaginating sutures placed 3 mm. apart. For the inner layer, 0 chromic catgut is used through all layers of the gut and securing a good bite of the esophageal mucosa. The outer layer is of 0 black silk and so placed as to invaginate the esophagus into the jejunum. The wound is then lightly powdered with sulfathiazole-penicillin mixture and closed with a Penrose drain.

Meanwhile an end-to-side anastomosis has been made between the short stump of jejunum left beyond the ligament of Treitz and the side of a convenient portion of jejunum.

A gastrostomy is made, using a mushroom catheter and bringing the catheter out 2 or 3 inches lateral to the paramedian incision.

The diaphragm is not sutured back to the costal margin and the peritoneum is very loosely closed around the jejunum as the latter enters the anterior mediastinum. The rest of the wound is closed in the usual manner.

The patient is fed intravenously for three days after operation, when gastrostomy feedings are commenced. Gastric suction is applied immediately for distention. Clear fluids are allowed by mouth after the second week and soft foods and solids after the third week.

CASE REPORTS

CASE 1.—Mrs. E. D., aged 50 years. On Sept. 23, 1948, thoracotomy revealed a carcinoma involving the lower esophagus and most of the stomach and infiltrating the pericardium, lung, and aorta.

Three weeks later an esophagojejunostomy was performed through the anterior mediastinum. An antiperistaltic tube was prepared by the method of Rienhoff and was a good color until drawn into the neck, where the end was blue and viability appeared doubtful. It was clear that excess tension had been applied, injuring the vessels of the arcade. However, after a few minutes the color improved slightly and the anastomosis was completed. At the end of the operation, the patient's blood pressure was 136/80 and pulse 100. Two days later she complained of a sense of oppression beneath the lower sternum, the pulse accelerated, and she died on the following day of gangrene of the jejunal tube.

CASE 2.—Mrs. S. B., aged 70 years. Patient admitted to the Vancouver General Hospital on Oct. 28, 1948, with a carcinoma of the lower third of the esophagus and secondary deposits in the cervical lymph nodes. She was very emaciated, weighing only 85 pounds.

Twelve days later a cervical esophagojejunostomy was performed. Secondary tumors were found in the celiac lymph nodes, liver, and mesentery. As in the first case, an antiperistaltic tube of jejunum was used and a gastrostomy was not done. Condition of patient at end of operation was good with blood pressure 130/90 and pulse 80. Two days later the neck incision was clean and so the Penrose drain was removed. Sips of water were commenced by mouth, but the patient vomited bile-stained fluid and continued to do so without letup. Eight days after operation both the neck and abdominal incisions were clean and sutures were removed, but the persistent vomiting commenced to produce feculent fluid. Two days later this fluid first discharged from the neck incision.

In the fourth postoperative week the abdomen was reopened. The jejunal tube was hypertrophied, and contracted firmly when touched. The jejunojejunostomy was well healed and widely patent, yet the bowel distal to it was absolutely collapsed. Obviously the stoma was not functioning yet no adequate reason could be seen. A second side-to-side jejunostomy was performed below the first and a catheter jejunostomy established for feeding lower down. The feculent vomiting continued and the patient died a few days later.

At autopsy the jejunal tube was viable. The fistula in the neck from the esophagojejunostomy was 5 mm. in diameter; otherwise the anastomosis was intact.

At the time it was felt that the vomiting and incomplete wound healing were the result of widespread tumor metastases. Unfortunately, the association of the vomiting with the aniperistaltic type of jejunal tube was not yet fully appreciated.

CASE 3.—Mr. M. J. McL., aged 69 years. March 1, 1949, patient was admitted to Shaughnessy Veterans Hospital and found to have a squamous carcinoma involving the lower 9 cm. of the esophagus. It was realized that a supra-aortic esophageal section would be required. A preliminary esophagojejunostomy was planned to be followed by a second stage for complete removal of the thoracic esophagus and the cardia of the stomach.

A cervical esophagojejunostomy was performed with a jejunal tube through the anterior mediastinum. An antiperistaltic tube was again used but in addition a catheter was inserted into the jejunum for feeding. At end of operation blood pressure was 123/70 and pulse 92.

Four days after operation his condition was good and clear fluids were commenced by mouth. The next day he began to complain of nausea and increasing pain and pressure in the upper abdomen. Various measures failed to give relief and he became increasingly distended and short of breath, and died on the eighth postoperative day.

Autopsy showed acute dilatation of the stomach, duodenum, and transplanted jejunum. There was no gas in the stomach which accounted for the failure to make a diagnosis. The jejunojejunostomy was patent and well healed but apparently not functioning. The neck wound was well healed but the esophagojejunostomy although intact was not safely healed, for although the esophageal muscle and jejunal peritoneum had adhered, the mucosal layers were not continuous (Fig. 8).

We were then forced to the conclusion that an isoperistaltic tube was essential to a well functioning jejunojejunostomy. In addition a gastrostomy is necessary for prolonged feeding to permit secure healing of the esophagojejunostomy.

CASE 4.—Mr. C. T., aged 43 years. Patient was admitted to the Vancouver General Hospital on April 14, 1949, having swallowed lye *five* weeks before. Barium swallow showed the esophagus occluded beneath the manubrium (Fig. 9, *A*). While being prepared for esophageal reconstruction an emergency operation was necessary for perforation of the stomach which was found to be shrunken and indurated as well as ulcerated. At the same time a catheter gastrostomy was made for feeding.

Ten days later a cervical esophagojejunostomy was constructed through the anterior mediastinum using an isoperistaltic tube and other measures as described above in our present technique (Fig. 9, *B*).

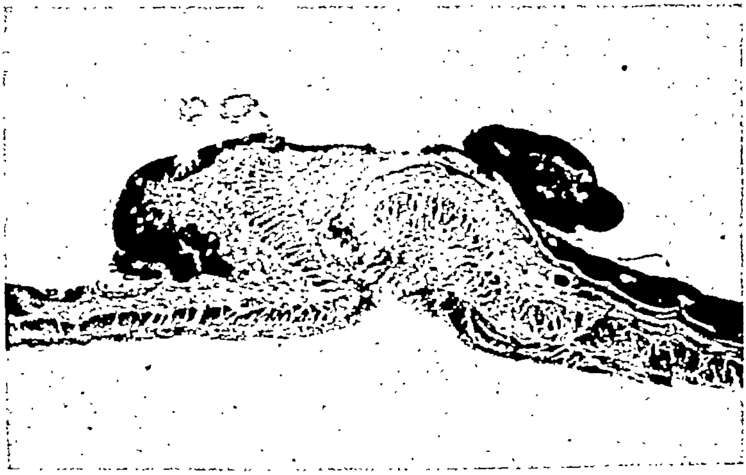


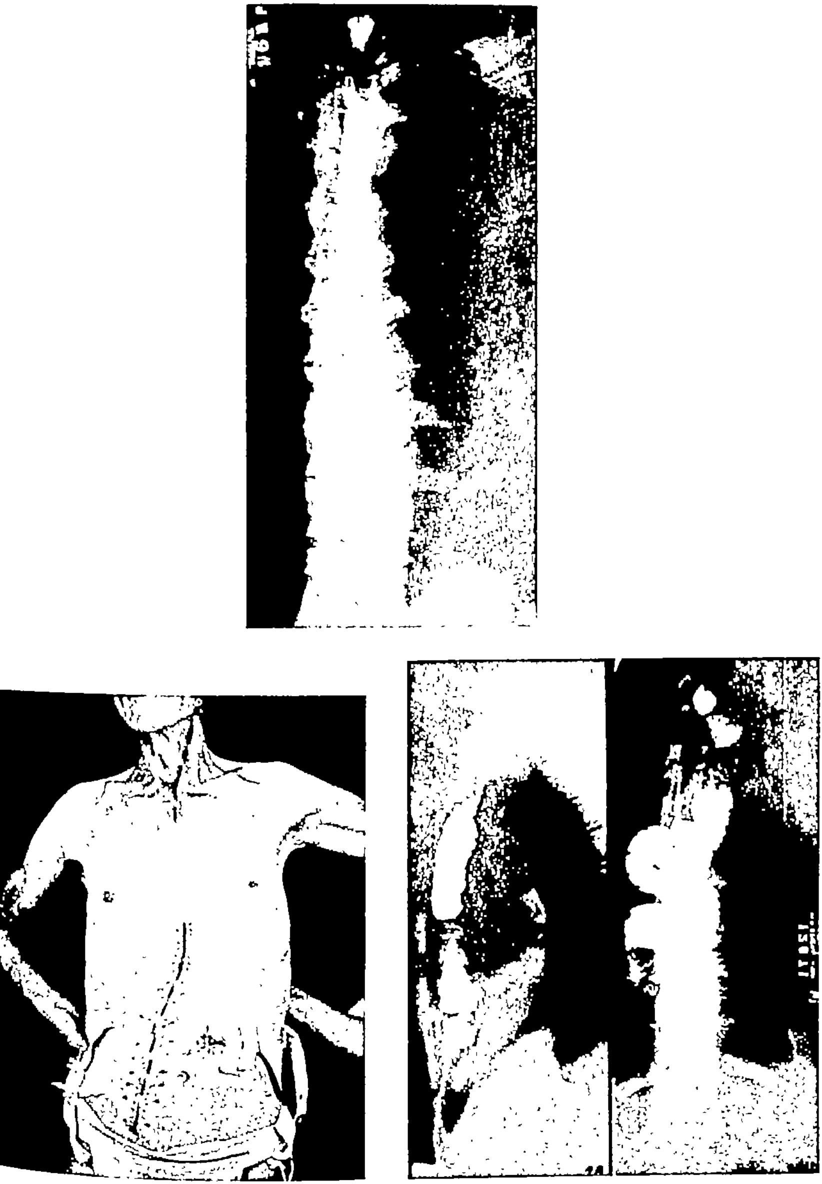
Fig. 8.—Longitudinal section at site of esophagojejunostomy showing extent of healing eight days after operation. The esophageal muscle and jejunal serosa have adhered but the gap in the mucosa remains.

A month later he was able to swallow fluids only. At esophagoscopy the invaginated edges of the esophagus at the anastomosis were found adherent to each other. They were readily freed with bougies and separated widely leaving a large lumen. A barium swallow five weeks after operation showed jejunal transplant in the anterior mediastinum functioning well (Fig. 9, *C*). Subsequently he has been on a full diet with only occasional difficulty in swallowing leafy vegetables.

In June he developed signs of a penetrating gastric ulcer and on June 13 a total gastrectomy was performed. The lower stump of the esophagus was sutured and invaginated. The excised stomach was extensively scarred and ulcerated from lye burns especially along the lesser curvature.

At present he is working full time on the farm, eats heartily, and weighs 180 pounds. The isolated esophagus has not caused trouble. It seems likely that the mucosa has been entirely destroyed.

CASE 5.—Mr. G. S., aged 69 years. Patient was admitted to the Vancouver General Hospital on July 3, 1949, with a carcinoma of the esophagus, ulcerating into the left main bronchus, and occluding the esophagus (Fig. 10, *A*). Patient was emaciated, weighed only 105 pounds, his heart was fibrillating, and there were râles at the base of both lungs.



B.

C.

Fig. 9 (Case 4).—*A*, Preoperative barium swallow. *B*, Three weeks postoperative, showing neck and abdominal incision and gastrostomy tube. *C*, Five weeks postoperative, barium swallow showing jejunal transplant in anterior mediastinum.

(1947) when streptomycin was begun. Although penicillin has been distinctly helpful, it has not been the panacea we thought it would be, because of the frequent presence of penicillin-resistant organisms. Our results have been distinctly better since streptomycin has been employed in conjunction with penicillin. In the 42 cases treated during the last three years, there have been 29 recoveries and 13 deaths following operation.

In order to reduce the mortality further, it seems to me that it is necessary for us to modify our previous philosophy regarding the multiple-stage plan which we formerly avoided. It used to be our endeavor to obtain esophageal continuity by direct anastomosis even at very long odds. If one takes such long chances because of too great separation of the segments, a certain number of the anastomoses will break down and the mortality in this group will be considerable. In the last year we have started the multiple-stage plan in several cases when an esophageal anastomosis did not seem advisable. It is planned to obtain intrathoracic continuity at a later date by esophagogastrostomy or by esophagojejunostomy, as described previously by Dr. A. W. Harrison or as described today by Drs. Robertson and Sarjeant. In our cases, three primary esophagogastrostomies have been done by other members of our staff, one of them by Dr. C. F. Storey being successful. By and large, however, this operation as a primary procedure in the infants without air in the stomach carries a high risk and, therefore, I feel that the safer plan is to tide such infants along with gastrostomy and cervical esophagostomy until such time as they can more safely withstand esophagogastrostomy or esophagojejunostomy.

The operative approach as described today by Dr. Potts, and earlier by Dr. I. A. Bigger, has much to be said in its favor, although I have not used it as yet, inasmuch as the right extrapleural approach with the resection of short lengths of three ribs posteriorly has given adequate exposure.

DR. LOGAN LEVEN, St. Paul, Minn.—It was a pleasure to hear Dr. Potts' and Dr. Robertson's papers. We have had some experience with tracheoesophageal fistula at the University Hospital in Minnesota. Since 1939 we have seen 77 cases, and in only 5 the operation was not carried out either because the patient died in the receiving room or the parents refused permission for surgery. In our earlier experience we performed a gastrostomy on 5 patients. This probably was worse than no operation at all, since it added to the regurgitation through the tracheobronchial fistula into the lungs. In our first cases we performed the so-called multiple-stage operation, doing 20 such cases. I believe that the multiple-stage operation will always have a place in the management of some of these cases. In the simple atresias without tracheoesophageal fistula, the distance between the segments of esophagus is usually so great that a primary anastomosis cannot be carried out, and the risk of bringing the stomach into the chest as a primary procedure is exceedingly great at this age. Accordingly, I believe the multiple-stage operation would reduce the mortality in such cases.

Of the 20 in which we performed a multiple-stage operation, 11 have survived. I am sure at the present time this mortality would be improved considerably. Of the 11 surviving, six have had reconstructions, five by using an antethoracic jejunal tube and one by an intrathoracic operation, bringing the stomach into the cervical region and performing a primary anastomosis. Dr. Richard Varco has performed these reconstructions with no mortality. The use of the jejunal tube antethoracically may have considerable merit. The stomach is left in the normal position with intact vagus nerves. The criticism of the undesirable cosmetic appearance could be corrected by division of the ribs and replacing the jejunal tube within the chest after it has been successfully reconstructed antethoracically, as Dr. Potts did with the stomach in his case. The risk of bringing the jejunal tube subthoracically would be considerably less than bringing it up through the thorax as a primary procedure. In none of our cases have we lost any of our jejunal tubes. However, an anastomosis of the jejunal tube to the cervical esophagus was not carried out as a primary procedure but performed after an interval of several weeks.

We have carried out primary anastomosis in 47 cases and have 30 that are living. The results in the last few years have been considerably better than was our initial experience. In the last two years we have performed 19 primary anastomoses, with 15 patients living and well. It is of considerable interest that these 19 cases have been done by seven different surgeons of the Surgery Department of the University of Minnesota Hospital.

We have used an incision in the right chest, removing the third or fourth rib in its entirety in all our cases since the first successful case in 1939, when we did a multiple-stage procedure, ligating the tracheoesophageal fistula extrapleurally. I feel that this incision gives very adequate exposure and agree with Dr. Potts that a satisfactory chest wall is the end result.

I should like to emphasize the limitation of fluids and, especially, the limitation of saline in the postoperative period. In most of our cases we perform a gastrostomy the day following primary anastomosis of the esophagus. In 10 cases we did not perform a gastrostomy, but I feel that it is a safety precaution which facilitates the feeding problem in these cases in the postoperative period.

In all our cases we have used cyclopropane, and in the last several years have used intratracheal anesthesia. In none of the cases have we had difficulty incident to the anesthesia.

DR. GEORGE H. HUMPHREYS, NEW YORK.—I am sorry I cannot give detailed statistics, but at the Babies' Hospital in New York we have had experience with approximately 50 of these procedures over the past ten years. The philosophy back of the procedure is interesting. I seem to have gone through exactly the reverse of Dr. Haight's change in philosophy. We started out by doing mostly multiple-stage operations, bringing the esophagus up into the neck and closing the fistula. We now try to anastomose them, even at long odds. I think that change in philosophy has been due to the difficulties in doing the secondary repair in these cases.

We do gastrostomies in all our patients. As Dr. Leven said, we feel that it is not always necessary when the repairs are satisfactory and the children can swallow probably very promptly. We know that is the case because the amount of mucus which is aspirated will vary with the patency of the anastomosis, and when the child does not have to be aspirated frequently the anastomosis is working well. However, we do feel it is safer not to feed early except by gastrostomy, and the dangers of parenteral over-hydration have already been emphasized.

We do not drain. We have drained in the past and have regretted it; we think sometimes drainage predisposes to leakage. Some leakage has occurred and has had to be drained secondarily, but if an anastomosis can be made satisfactorily and gastrostomy is done early, I think there will be very few leaks.

I would like to point out one fact which we have found out to our cost, which is in contrast to what Dr. Potts mentioned. That is, that absence of air in the stomach and intestines does not mean absence of a fistula. Some of these fistulas may be very small, the child may be very weak and does not have a strong enough cry or cough to force air through the fistula. In such a case there would be no air, especially in the first few days of life, in the intestinal tract, yet a fistula may be present.

Our mortality is high, approximately 30 to 35 per cent. Technical considerations play a part, but the prime factors are those emphasized by Dr. Potts, prematurity, failure to make the diagnosis early, and aspiration pneumonia.

DR. HARRIS B. SHUMACKER, JR., Indianapolis.—I should like to comment briefly about one aspect of the problem of utilizing the jejunum; namely, that of its blood supply. I think we all are in agreement that there are many cases in which the jejunum seems to be the ideal structure for use in esophageal reconstruction. Since the days when Roux first proposed the use of this organ, however, the one feature which has plagued operators has been the inadequacy of the blood supply of the freed and mobilized limb. It seemed to me that perhaps experiences with peripheral circulatory disorders might offer a suggestive lead. We know that the gradual occlusion of a major arterial stem is often tolerated without loss of tissue when the sudden occlusion of the same artery would ordinarily produce massive gangrene. Following this lead, Dr. Battersby and I have recently completed some animal experiments and one human application which I believe will go a long way toward solving this problem. We have found that loops of jejunum of a given length when freed of their arterial blood supply in one stage inevitably lead to gangrene and rupture, but maintain adequate circulation if the division of the arterial supply is staged; first, dividing every other artery and, at a later date, dividing the intervening ones. If we divided in one stage the blood vessels to loops of the jejunum of the dog ranging from 25 to 40 cm. in length, gangrene and rupture inevitably took place. In contrast, if we divided every other vessel and, a week or ten days later, divided the intervening ones, we had segments as long as 55 centimeters maintain good circulation. Indeed, by using three stages in one animal we obtained a Roux-Y limb, which was almost 100 cm. long and which was successfully transplanted into the neck.

I think the results are well illustrated in two lantern slides which I should like to show. In the rat, if one ligates four consecutive jejunal arteries, inevitably the intestine immediately becomes cyanotic, as is illustrated in the first slide, and it subsequently becomes gangrenous and ruptures. As is shown in the next slide, a Roux-Y can be constructed and six consecutive vessels ligated in two stages with maintenance of good circulation.

In one human being with a total esophageal stricture from lye injury, this principle has worked extraordinarily well. A Roux-Y jejunal limb was made and some of the vessels divided; ten days later the remaining vessels were divided and the jejunum transplanted; a week later the anastomosis was performed.

DR. OSLER A. ABBOTT, Atlanta.—I should like to comment on two aspects of the tracheoesophageal problem. We are becoming increasingly convinced that Lipiodol should not be used in the study of these patients because of the frequency with which it may spill over into the tracheobronchial tree and carry with it a consideable amount of inspissated material from the upper esophageal segment, which is a potential serious danger. We are trying to emphasize to pediatricians in our area to make the diagnosis by insertion of a catheter alone, and if Lipiodol is insisted upon, that a preliminary clean-out of the upper esophageal stump be done. We have had several x-ray pictures sent to us showing Lipiodol spilling over from a blocked upper stump into the tracheobronchial tree.

I should like to mention that we have had experience with two patients of the same type as Dr. Haight presented, without atresia, but with tracheoesophageal fistula of congenital type. One of these was discovered, and operated upon successfully, within the first six weeks of life. We also feel that one of the greatest help which one of our staff obtained recently from a visit to Dr. Haight's clinic, is the importance of keeping the child on the side to be operated upon, for twenty-four hours prior to operation, so that all the inflammatory and other trouble in the lung may be confined to that area. This has been of tremendous value to us and, I think, deserves emphasis.

DR. CONRAD LAM, Detroit.—I thought there might be some interest in a progress report on the two boys whose pictures I showed two years ago in Quebec. If you recall, the continuity of the esophagus in each was obtained by the somewhat outmoded method of skin tube construction. The oldest child I have not seen professionally, but have seen socially a few times; he is now in second grade in school and apparently is suffering no psychologically bad effects from his antethoracic esophagus. I should like to ask Dr. Potts if he thinks this esophagus could be transplanted to an intrathoracic position by his method.

The second child, I must report, is still alive and healthy, but about six months ago he had what appeared to be acute follicular tonsillitis, and the inflammation spread down into the chest about the skin tube. I had to insert a tube for feeding for a few days. This little opening has persisted as a sinus and shows little tendency to close, although the only thing that is necessary for this boy to eat three meals a day is for the mother to put a small piece of adhesive tape over it.

DR. JULIAN JOHNSON, Philadelphia.—There is one point I would like to mention. I am sure that a good many people over the country are doing these tracheoesophageal fistulas by the transpleural approach. We have been using it for the last year or eighteen months at Children's Hospital in Philadelphia. Making a fourth intercostal incision, we go transpleural and the operation can be done much more quickly, usually being completed in an hour and fifteen minutes to an hour and a half. It seems to us that the only risk is that there might be a leak at the point of anastomosis, resulting in generalized empyema. We have had one leak of this type; it has not produced a generalized empyema, however. By the time the leak occurred there was apparently sufficient sticking of the lung around that area so that the tube which had been placed in the manner described by Dr. Potts took care of the leak satisfactorily. We think the operation can be done much more quickly; we think the children do not have as much respiratory difficulty postoperatively and, all in all, in our short experience we have been favorably impressed.

DR. R. H. SWEET, Boston.—There are one or two points on which I would like to comment. One is about the use of the stomach to restore continuity in these multiple-stage cases of which Dr. Potts and others have spoken. It seems to me that his experience has quite amply demonstrated that the better place for the stomach is in the chest rather than in the subcutaneous area. This, of course, can be done as a primary procedure and, in my experience, has worked well. I would like, however, to lend emphasis to some of the comments this morning, that it is unwise to do that operation in an infant, because of the disparity in size between the enormous fluid and gas filled stomach and the volume of the thorax. In my hands, at least, it has not been a successful procedure. I much prefer to delay and use the stomach later.

The other comment has to do with the use of the jejunum. The essayists and commentators this morning have brought up some of the difficulties. Dr. Robertson referred to the experience I had with a patient presented before this Association in the discussion of Dr. Harrison's report, which I believe lends weight to the wisdom of Dr. Harrison's point of view that the lower end of the jejunal segment should be implanted into the stomach. That patient behaved very much like a person who had a jejunostomy performed for feeding, and we were unable to maintain a satisfactory degree of nutrition. She lost weight at home and the only way we could keep her in good condition was to keep her under supervision in the hospital. At a later date I reoperated upon her and transected the loop of jejunum above the jejunojejunostomy, implanting the proximal end of the transected portion into the fundus of the stomach. Since then she has maintained a satisfactory nutritional state.

DR. POTTS (closing).—Many interesting and valuable points have been brought out in the discussion. Dr. Haight asked about the virtues of resection of a rib instead of the subperiosteal resection of three ribs. We believe that we get better exposure in that way, because the ribs of an infant are extremely flexible. When one rib is removed a small mastoid retractor will easily spread the ribs widely. In closing the wound these very flexible ribs can be brought together; if the fourth is resected the third can be sewed to the fifth and thus furnish a solid chest wall against which the child can breathe.

I was glad to hear the tendency toward intrathoracic transplantation of the jejunum as an esophagus. I think Robertson's suggestion of putting it behind the sternum is an excellent one. After all, these children put themselves unwittingly into our hands and are entirely helpless in what we do. The parents cannot evaluate our advice. I do not believe that a girl should have an antethoracic transplantation of anything—jejunum or anything else. It is going to be a very peculiar deformity at the age of 16 years. I question whether it should be done on a boy. After all, to live nobly, as Dr. Eloesser has said, is such an extremely important thing. *The psychologic effect of having such an abnormal* structure on the front of the chest, when the youngster goes to high school and college, I believe will be disturbing. I am sure all efforts should be made toward intrathoracic construction of esophageal tubes.

DR. ROBERTSON (closing).—I wish to thank Dr. Haight particularly for his indication that he may be tempted to use a jejunal transplant in the anterior mediastinum. Regarding the problem of nutrition in these patients, as brought out by Dr. Sweet, we have anticipated difficulty in that regard, but so far the two patients that have done well have gained a great deal of weight; one man has gained about sixty pounds and the other man, with Hodgkins' disease, has gained twenty pounds, and we feel we will reserve the transplant into the stomach for patients who fail to gain weight.

Postoperative x-ray films on these patients show some retrograde filling of the stomach. I believe Dr. Harrison also had that experience.

USE OF THE BURNS VALVE AS A SIMPLE RESPIRATOR FOR INTRATHORACIC SURGERY IN THE DOG

JOSEPH T. DAMERON, M.D.* (BY INVITATION), AND DAVID G. GREENE, M.D.†
BUFFALO, N. Y.

THE efforts of members of the surgical staff in this laboratory were handicapped by the lack of a simple respirator which did not produce anoxia and a progressive increase in carbon dioxide content of the blood when attempting various intrathoracic operations in the dog.

Use of the "windshield wiper" respirator[1] used in many laboratories resulted in the death on the table of many of our animals from anoxia and ventricular fibrillation. This machine operates by giving a sudden blast of air into the trachea for inflating the lungs. The degree of deflation of the lungs depends upon the amount of leakage around the intratracheal tube. The intratracheal pressure during inspiration and expiration is uncertain. Sustained intratracheal pressure during expiration greater than atmospheric pressure impedes the venous return to the heart and consequently cardiac output. This laboratory has had no personal experience with either the Crafoord[2] or Mautz[3, 4] machines. Both are expensive and require a skilled attendant. Gibbon's data[5] suggest these two machines do not always overcome a tendency for a rise in the arterial CO_2 tension. Gunkler and Mahoney[6] have recently described a complicated respirator for intrathoracic surgery without giving either blood gas values or the intratracheal pressure during inspiration and expiration.

The Burns valve[7] was developed during the last war for the Air Force as a respirator. The mechanics of the valve may be found in Burns's original paper. The purpose of this paper is to report: (1) the adaptation of this valve for anesthesia during intrathoracic surgery in the dog and cat; and (2) to present data on the arterial blood gas values in the dog, when operating the valve with either compressed air or 100 per cent oxygen.

METHODS

A. *Description.*—Over 150 dogs weighing between 12 and 75 pounds have undergone prolonged intrathoracic operations using the method to be described. This device has also been adapted to the cat. The preoperative medication in the dog consists of morphine sulphate 0.015 Gm. and atropine sulfate 0.0004 Gm. given intramuscularly one hour pre-

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†Research Fellow, Department of Medicine.

operatively. The animal is anesthetized lightly with either pentothal or pentobarbital by the intravenous route. A No. 30 Colby hemostatic catheter, which may be found on most urological services, is inserted into the trachea and the bag inflated for a tight seal. We have found this catheter to make an excellent intratracheal tube. It has a durable bag which is not easily punctured. A No. 18 Foley catheter with the tip cut off is easily adaptable as an intratracheal tube for the cat. An ether bottle is interposed between the Burns valve and the intratracheal tube. If the line pressure is set to cut off at a pressure of 12 to 14 cm. of water or less, the lungs will rhythmically inflate 14 to 20 times per minute to the desired pressure, and supplementary ether may be given as necessary. The 11 animals in which blood gas analyses were made were completely anesthetized with pentobarbital, since slight traces of ether might invalidate the blood gas determinations. Fig. 1 demonstrates the apparatus as used.

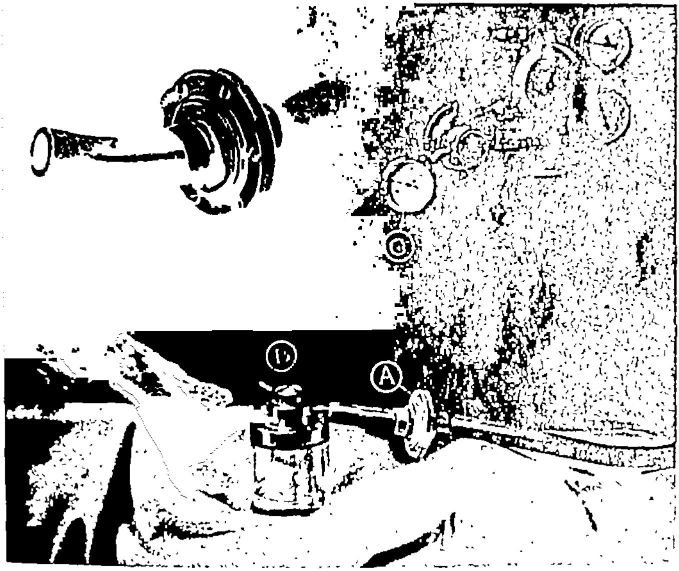

Fig. 1.—The apparatus as used: *A*, Burns valve. *B*, Ether bottle with regulator. *C*, Pressure gauge and regulator for maximum pressure.

B. *Blood Gas Analysis.*—Arterial blood was obtained from the femoral artery of 11 dogs. In the 7 dogs in which compressed air was used, the partial pressures of carbon dioxide and oxygen (pCO_2 and pO_2) were obtained by the bubble technique of Riley and associates.[8] In 4 dogs in which 100 per cent oxygen was used, arterial blood samples were analyzed for oxygen and carbon dioxide content, and oxygen capacity by the method of Van Slyke and Neill,[9] and the pH was measured with a glass electrode. From these figures the pCO_2 was calculated using the nomogram of Singer and Hastings[10] for human blood. In all 11 experiments, one sample of arterial blood was taken after the dog was premedicated with morphine and anesthetized with pentobarbital prior to opening the chest and connecting the respirator. This is labeled control sample. Subsequent samples were obtained after the chest had been opened and the respirator functioning for one and one-half to three and one-half hours.

The intratracheal pressure in dog No. 208 was recorded graphically, using a Hathway blood pressure recording system, and is reproduced in Fig. 2.

RESULTS

The Burns valve has been used successfully in over 150 prolonged intrathoracic operations in the dog and in 6 cats. It has eliminated the need for an anesthetic attendant in the operating room. No dog has died on the operating room table while the valve was in use, a record which is in striking contrast to our experience with other methods.

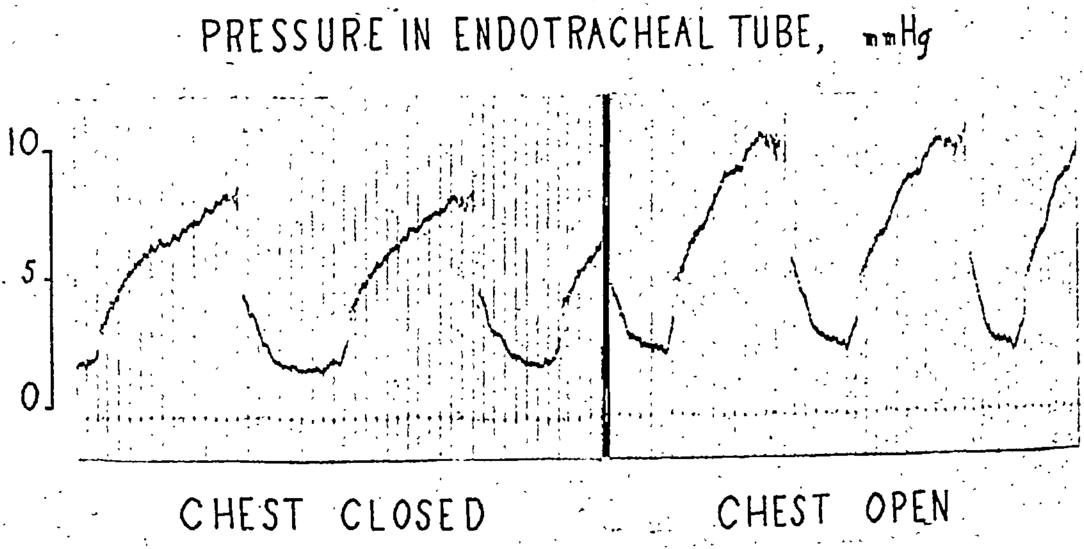

Fig. 2.—Variations in pressure throughout the respiratory cycle, measured in the intratracheal tube. Time lines indicate 0.1 second intervals. Dog 208.

The partial pressures of carbon dioxide and oxygen are recorded graphically in Fig. 3 and a detailed analysis of the blood is given in Table I. One will note that when the respirator was operating on compressed air, approximately 21 per cent oxygen, the carbon dioxide tension of the blood never rose above normal limits and in most instances there was a decrease. When the respirator was operated on 100 per cent oxygen, the tendency to blow off carbon dioxide excessively was not noted. In 2 dogs a high carbon dioxide tension was noted with the use of 100 per cent oxygen. Acidosis was noted after the use of the respirator and 100 per cent oxygen in all 4 dogs in which the pH of the arterial blood was measured. This had decreased in comparison with the control value in 2 dogs, in one it developed although the control value was normal and in one it remained essentially the same as the control value.

The shape of the intratracheal pressure curve, Fig. 2, shows a fairly gradual rise in pressure during inspiration, and a rapid drop at the beginning of expiration followed by a more gradual decline which never reaches atmospheric pressure. The inspiratory phase is longer than the expiratory phase of respiration. Although the peak inspiratory pressure is higher in the tracings taken with the chest open, the general shape shows little change. The increase in peak pressure is due to a slight change in line pressure between the two tracings.

TABLE I

CHEST CLOSED, NO RESPIRATOR, ANESTHETIZED (CONTROL SAMPLE)			CHEST OPEN, WITH RESPIRATOR			
			21% OXYGEN		100% OXYGEN	
DOG NUMBER	pCO₂ (MM. Hg)	pO₂ (MM. Hg)	pCO₂ (MM. Hg)	pO₂ (MM. Hg)	pCO₂ (MM. Hg)	pO₂ (MM. Hg)
111	52	51	15	105	-	-
171	43	93	25	111	-	-
173	40	45	38	61	-	-
135	50	80	45	71	-	-
162	46	78	37	66	-	-
164*	34	67	9	88	21	145
187*	41	84	28	69	34	147

					100% OXYGEN			
	CO₂ CONT. (VOLS. %)	pCO₂ (MM. Hg)	pH	O₂ SAT. %	CO₂ CONT. (VOLS. %)	pCO₂ (MM. Hg)	pH	O₂ SAT. %
201	40.6	64	7.16	82.4	40.3	46	7.20	100-
231	43.3	57	7.17	83.4	35.0	49	7.28	100+
207	43.4	36	7.43	81.8	43.8	65	7.15	100-
217	47.0	60	7.18	83.6	44.7	60	7.16	96.6

*Dogs maintained on respirator with compressed air (21 per cent O_2) for two hours and second sample then obtained. The third sample obtained after further maintenance on respirator for thirty minutes with 100 per cent O_2. Approximate tensions estimated by Riley technique.

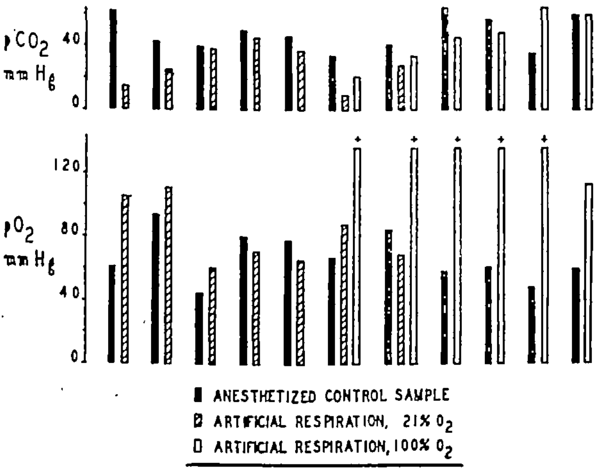

Fig. 3.—Blood gas results expressed in terms of carbon dioxide and oxygen tensions, either measured directly or calculated. Plus marks indicate that oxygen tension was 145 mm. Hg or greater. Normal values for carbon dioxide tension 36 to 48 mm. Hg, for oxygen tension 80 to 100 mm. Hg. The graphic illustration was obtained on eleven animals, each group of columns having been obtained on a separate animal.

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DISCUSSION

DR. F. R. MAUTZ, Cleveland.—My interest in mechanically controlled breathing also originated in the surgical laboratory, and about twelve years ago we began to use mechanically controlled breathing in clinical thoracic surgery. We found some differences between the dog and man due, presumably, to such factors as relative size, vigor of the pulmonary reflexes, anatomic differences in the pleural membrane, and such pathologic processes as pleural thickening, adhesions, and pulmonary fibrosis, with emphysema sometimes present in man. As a rule these pathologic processes were not present in the dog.

In our earlier experiences these factors gave us some difficulty in taking over mechanical control of breathing without resorting to a depth of anesthesia that might be detrimental. However, following the introduction of curare, our clinical problem was greatly simplified, and at present a future seems assured for mechanically controlled breathing. We have now used mechanically controlled breathing in approximately 300 patients, controlling respiration from the time just before the pleura is opened until the pleura is closed, and we feel that patients can be kept in a better physiologic state for procedures of considerable duration by this method than by other methods of management. I have no quarrel with the anesthetist who wants to get his exercise by manual compression of the breathing bag, provided he will supply the necessary amount of pulmonary ventilation. I think in the future we must be concerned with getting the amount of pulmonary ventilation necessary not only to get oxygen into the blood, but also to adequately clear the blood of carbon dioxide. I feel quite sure that we are going to see improvements in mechanical equipment and, by further evaluation of the actual job of ventilation being done, I think we are going to find that mechanical types of breathing will be of considerable value, especially in prolonged operations. I do not think we need worry about accumulation of carbon dioxide in short procedures; it is in the long procedure that we must be concerned.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—In my opinion it is a fundamental phase in intrathoracic surgery that has been touched upon by the previous speakers. Mechanical control of respiration as soon as the chest is opened, in our experience, is the only method that gives respiration similar to the physiologic. As you know, we have used this type of respiration on my service for more than fifteen years in all our clinical cases, with most satisfactory results. It was based upon laboratory studies undertaken in the early thirties. These showed that mechanically controlled respiration, with an inspiratory phase similar to the one the animal had when breathing spontaneously, and an expiratory phase without any increase of pressure so that the expiratory gas could flow out freely, gave the best results when investigating the arterial oxygen tension and the content of carbon dioxide in the blood, as well as the values of the pH.

We have used mechanically controlled respiration now in several thousand clinical cases, and we have had no complications from using this method. It has been very gratifying to me to find that in this country during the last few years, an increasing interest has been shown in using this type of respiration for prolonged chest operations. I believe that the retarded development in this field in your country is due to the two schools of anesthesia from Madison and Boston, which emphasize that the anesthetist must follow the spontaneous respiration very closely in order to judge the condition of the patient. I am convinced, however, that there is no reason whatsoever not to paralyze all the respiratory muscles and to regulate the respiration of the patient mechanically during the time of an open chest operation, which method certainly is superior to any other.

DR. PAINE (closing).—I think one can appreciate the value of this valve in an experimental laboratory. We have had no dog die of anesthesia in the last 150, since this instrument has been used. We have been able to dispense with an attendant to take care of the anesthesia; the thing is set up, then one scrubs and goes ahead. We have been trying to get our anesthetists in Buffalo to use this clinically, with some reluctance on their part. Maybe they think they will soon not be needed. Probably 40 or 50 per cent oxygen would be better than 100 per cent.

I might just show you the fourth slide, which shows the interior of this little valve; it is an ingenious affair. Anyone who is interested can purchase this machine from the Mine Safety Appliance Company; they did have an office here in Denver.

THE DEVELOPMENT OF, AND CERTAIN CLINICAL APPLICATIONS FOR, A PORTABLE MASS SPECTROMETER

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RALPH T. KNIGHT, M.D., E. B. BROWN, JR., PH.D., AND
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MINNEAPOLIS, MINN.

RECENT technical advances have made possible an immediate assessment of the blood oxygen saturation and ether and oxygen concentrations in the inhaled gaseous mixture. These several devices supplement the anesthetist's sense of clinical judgment in the care of his patient. However, the instantaneous evaluation of alveolar carbon dioxide tension in the anesthetized patient still remains an area of confusion and recurring concern to the conscientious anesthetist, and more important, a grave potential hazard to the patient. Many attempts of limited success have been made to record the onset and duration of hypercapnia, but to date the interference introduced by those mixtures of anesthetic gases commonly used has prevented accurate, frequent, and rapid analyses for carbon dioxide. The problem of hypercapnia has recently been emphasized by both Beecher and Stormont.[1, 2] The former stressed the importance of this problem, particularly in thoracic surgery where the issue is often additionally complicated by an associated diseased respiratory system. His studies reported an average increase of the alveolar carbon dioxide concentration to 13.7 per cent in 16 pneumonectomy cases. This rise was associated with an average drop in the blood pH to 7.09. The Henderson-Hasselbalch equation was utilized for calculation of the alveolar carbon dioxide value after measuring the arterial blood pH and carbon dioxide concentration. Though such physicochemical methods are very accurate under normal conditions, the time involved in analyses and the necessity for anaerobic arterial blood samples as well as the errors introduced by the presence of anesthetic gases limit their widespread use as clinical tools for the anesthetist. The purpose of this paper is to present an alternative method for resolving certain of these difficulties.

At the University of Minnesota a continuously recording portable mass spectrometer has been developed by one of us (A. O. N.) for use in the operating rooms and physiologic laboratory as a rapid recording gas analyzer. This electronic device (Fig. 1) is capable of quantitatively analyzing the composition of a mixture containing five different gases. Every twenty seconds the process is repeated with an accuracy within 1 per cent. The presence of anesthetic gases introduces no measurable error. An instrument such as this should be an asset to the anesthetist, for it would allow him to obtain immediate knowledge of

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carbon dioxide concentration in the exhaled mixture as well as the amount of anesthetic gas in the system. He is therefore in a more favorable position to diagnose hypercapnia at its incipiency, to take the necessary corrective measures.

The mass spectrometer has been used for about thirty years by physicists in their study of the elements. It has been used extensively in industry as a leak detector and analyzer of unknown gas samples. However, biologists have been slow to adapt this method to their problems. It has served investigators as a stable isotope analyzer in the clarification of metabolic processes. The specific shortage of portable units and the relative unavailability of other models capable of analyzing a continuously changing gas sample has hampered work in this field. Except for the reports by Nier and associates[3] on continuous analysis of process stream contaminants in the Oak Ridge gaseous diffusion plant, and Kydd's study of CO_2/O_2 concentrations during alveolar carbon dioxide sampling,[4] no reports have appeared in the literature about a mass spectrometer capable of continuous gas analysis when the composition of the mixture is rapidly altered.

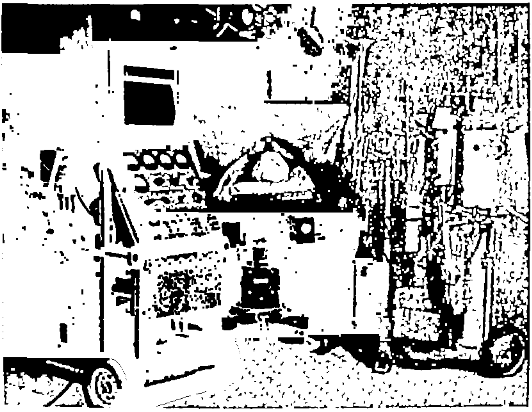
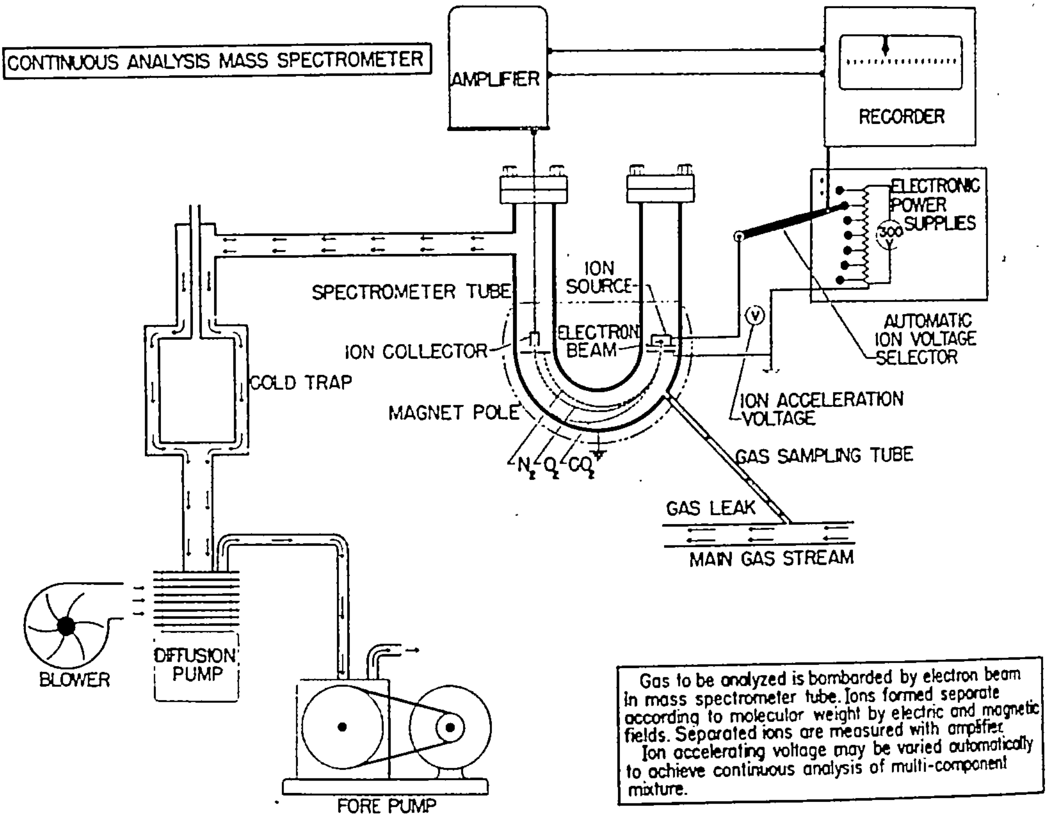


Fig. 1.—A picture of the mass spectrometer in the operating room.

The mass spectrometer used for the study being presented was designed to provide a portable instrument capable of rapid, continuous, automatic, quantitative recording of the components of the gas stream delivered to it. Fig. 2 illustrates schematically the basic features of this instrument. A sample of gas is drawn into an evacuated U-shaped chamber through a graduated leak and gaseous ions are formed by the electron beam. The trajectory of an ionized particle is dependent upon: (1) the molecular mass of the ionized particle, (2) the speed of the particle passing through the tube, (3) the amount of magnetic force acting upon the particle. With the magnetic force constant, the speed of specific particles passing through the tube is varied cyclically by changing the difference of potential across the two slit plates. As a result of this cyclic variation, each component beam of ions arrives systematically at a common ion collector. The current carried by these ionic charges is then amplified so as to be recorded by a standard commercial six-point potentiometer such as is commonly used for recording temperatures.



Gas to be analyzed is bombarded by electron beam in mass spectrometer tube. Ions formed separate according to molecular weight by electric and magnetic fields. Separated ions are measured with amplifier.

Ion accelerating voltage may be varied automatically to achieve continuous analysis of multi-component mixture.

Fig. 2.—A very much simplified schematic design of the basic principles of the action of the continuously recording mass spectrometer.

METHOD

The patients were anesthetized with ether, nitrous oxide, pentothal curare or a combination of all three agents. The preanesthetic medication was Nembutal, morphine sulfate, and atropine with the dosage regulated according to the age and physical condition of the patient. Thoracotomy cases were regularly placed in a semiprone position on a straight table. An intratracheal tube with an attached inflatable cuff was inserted so that manual ventilation could be performed. This assisted respiration was carried out intermittently in all of the cases anesthetized with pentothal curare, especially thoracotomy cases; here it was a routine procedure.

Following intubation the patient was connected to the mass spectrometer in the circuit shown schematically in Fig. 3. As illustrated, a continuous gaseous sample was withdrawn from the trachea—via a small bore polyethylene catheter threaded into and beyond the intratracheal tube to the vicinity of the carina. Circulation through this circuit was maintained by means of a small, leak proof, air blower of sufficient capacity that the lag time between patient and spectrometer was about 90 seconds.

Prior to each testing period the mass spectrometer was calibrated against a gas of known composition; at hourly intervals during the procedure and at the conclusion of surgery, it was rechecked for possible drifting. Rarely was any significant variation detected.

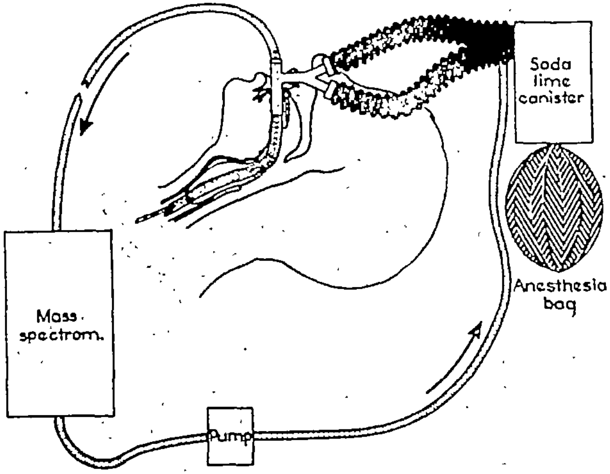


Fig. 1.—Schematic illustration of the sampling system used in the operating room to supply the mass spectrometer with a continuous stream of gas from the trachea of the patient.

An uninterrupted record rather than mere spot sampling was secured in each case. Peak *accumulations of carbon dioxide and their related effects* were more recognizable by virtue of an unbroken observation of these events. To avoid unsolicited cooperation from the anesthetist and to eliminate any explosion hazard the mass spectrometer was positioned at a distance of several feet from the anesthetic field. Since the toxicity of high alveolar carbon dioxide concentration probably rests chiefly on acidotic qualities, it seemed appropriate to correlate the carbon dioxide values with simultaneous blood pH levels. A control arterial sample was therefore drawn preoperatively under local anesthesia from the femoral artery. During the operative procedure a sample of blood was obtained either from an exposed artery in the operative field or from the radial artery. The pH determinations on these samples were made with a specially designed constant temperature glass electrode meter shown to be accurate to 0.01 pH units.[5] In the interim between sampling and analyzing, the blood was chilled to about 0° C. so that a reduction in pH due to glycolysis did not occur.[6]

RESULTS

In order to determine the accuracy of the mass spectrometer as a quantitative carbon dioxide analyzer and to evaluate the usefulness of the instrument as it was to be used, in indicating alveolar carbon dioxide concentration, preliminary experiments were performed in the laboratory. Two dogs were anesthetized with Nembutal and a continuous sample of respiratory gas discharged through the spectrometer in the manner illustrated in Fig. 3. In the absence of an interfering anesthetic gas the carbon dioxide concentrations could be checked periodically for agreement with a Scholander gas analysis of the same mixture.[7] Numerous tests were carried out and it was demonstrated that the two methods coincided within 0.5 per cent, that is, if the Scholander analysis gave a value of 10 per cent carbon dioxide the value obtained from the mass spectrometer would be between 9.5 and 10.5 per cent.

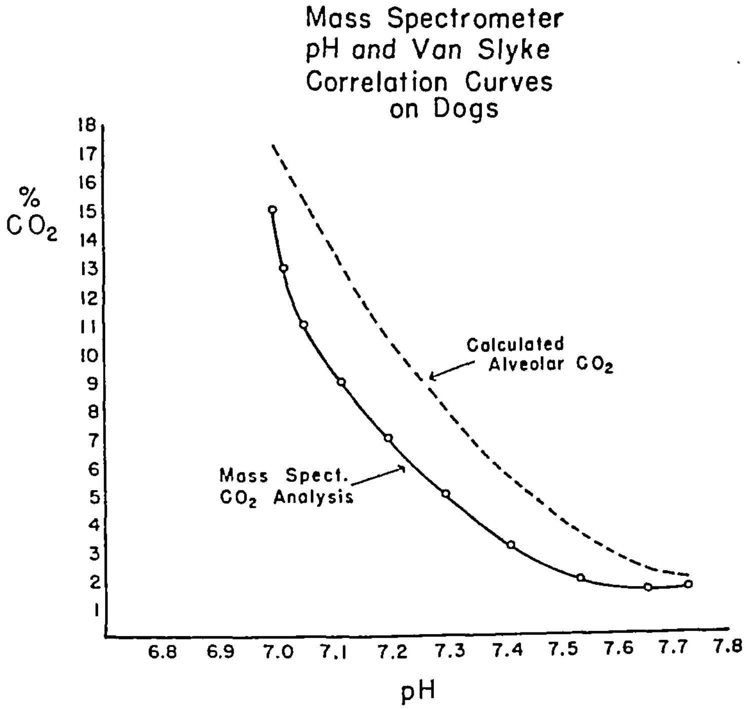


Fig. 4.—pH—CO_2 correlation curves of mass spectrometer recordings and simultaneous alveolar CO_2 per cent as calculated from arterial blood pH and CO_2 content.

Comparison between the carbon dioxide values as recorded by the mass spectrometer using the sampling method outlined previously, and the alveolar air carbon dioxide concentrations were made possible by calculation of the latter value from arterial blood pH and total carbon dioxide content utilizing the Henderson-Hasselbalch equation.*

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*In this equation with three interrelated variables, if any two of these become known the third can be readily calculated.[8] The equation is set up as follows, in order to determine carbon dioxide tension when the arterial pH and total carbon dioxide content have been measured (total carbon dioxide content measured by method of Van Slyke and Neill[9]):

$$pCO_2 = \frac{\text{Total } CO_2}{0.1316 \times 0.510\ (10^{pH - pK'} + 1)}$$

A respiratory acidosis due to excess carbon dioxide was induced in the dogs by removing the soda lime canister; alkalosis was produced by manual ventilation until a state of acapnia occurred. Arterial blood samples were drawn from the femoral artery during various stages of these procedures. Fig. 4 shows the variation of carbon dioxide concentrations and pH. The consistent difference between the mass spectrometer carbon dioxide concentration values and the calculated alveolar carbon dioxide concentrations, it seems reasonable to presume, is more likely an expression of the sampling technique used rather than any inherent error in the analysis. Because sampling is continuous throughout both inspiration and expiration, there is undoubtedly mixing of the true alveolar sample with dead space air and inspired air, whereas a truer alveolar air sample could be obtained only with elaborate sampling devices. Therefore, one would predict that carbon dioxide concentration would be less in the mass spectrometer sample which is obtained partially from both phases of respiration. This is borne out by the results given in Fig. 4. The parallelism of contour between the two curves implies a correlation which should allow a close estimation of the alveolar carbon dioxide concentration when the mass spectrometer reading is known.

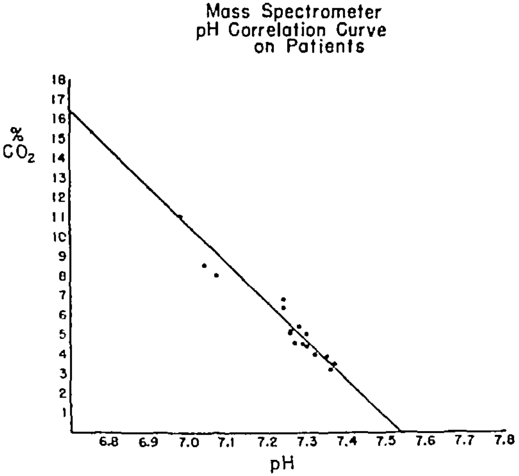

Fig. 5.—Tracheal air per cent CO_2 recorded by the mass spectrometer plotted against the pH of simultaneously drawn arterial blood from patients undergoing surgery.

Fig. 5 illustrates the relation between the mass spectrometer records and some pH values obtained during surgery. The degree of accord is indicated by the interpolated line. Our inability to secure sufficient analyses with low arterial pH values hardly justifies any attempt at statistical treatment of these data. However, the real correlation seen from pH 7.37 to 7.25 permits the assumption that this method is a relatively accurate index.

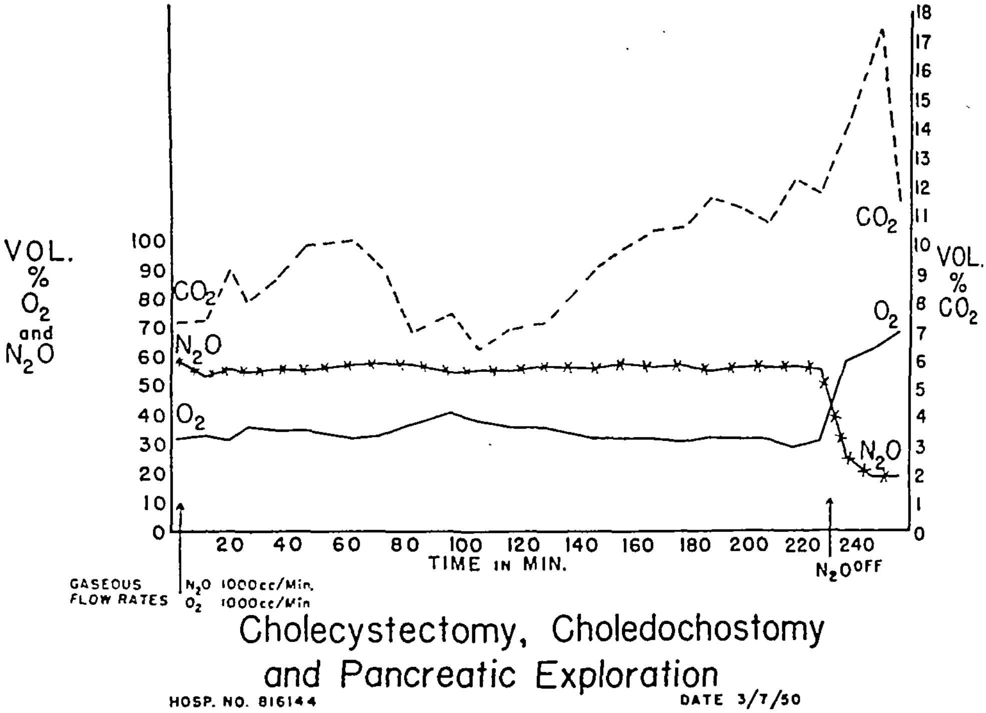

Fig. 6.—Results of a mass spectrometer recording. Note that the CO_2 values listed along the right ordinate are on a different scale from the O_2, N_2O values shown along the left ordinate. The small figures under the chart labelled N_2O and O_2 flow rates were values taken from the gas flow meters on the anesthesia machine.

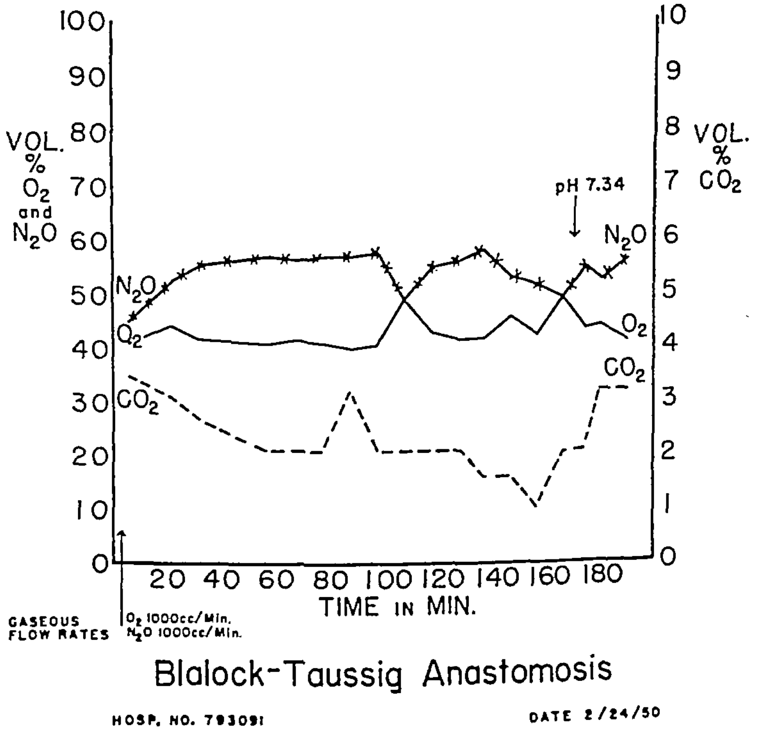

Fig. 7.—This replotted mass spectrometer record shows the low values encountered in a patient with compensated alkalosis. The arrow designates the point at which the arterial blood sample was drawn for pH analysis.

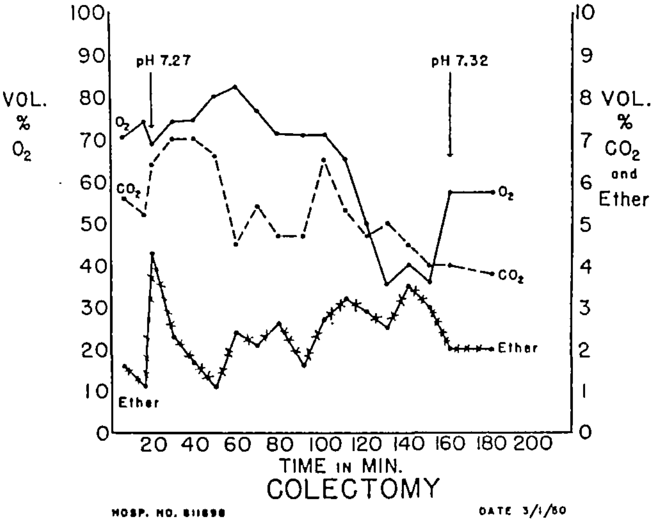

Fig. 8.—Mass spectrometer results on a patient anesthetized with ether. Note that the ether concentration is plotted on the same scale as the CO_2. For the most part the patient was carried with an ether concentration of 3 per cent or less. This is typical of most of the cases analyzed.

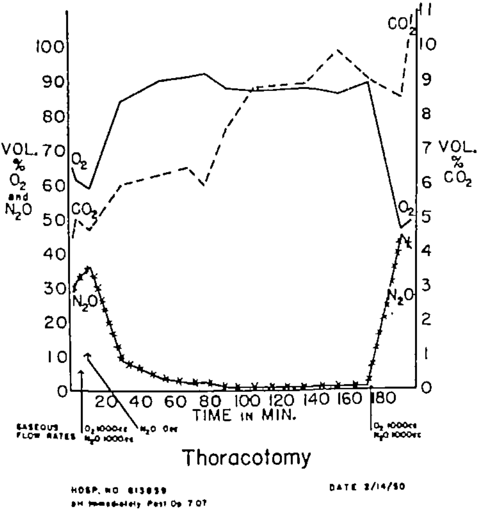

Fig. 9.—Mass spectrometer results on a thoracotomized patient. The neoplasm found was inoperable.

Figs. 6 through 10 are condensed reproductions of some of the recordings obtained. It should be remembered that 3 to 3.5 per cent carbon dioxide is a normal level for the sampling system employed.

On one occasion the carbon dioxide rose to 17.3 per cent, as is illustrated by Fig. 6. This is the highest value observed during the present series of experiments. Unfortunately no pH determinations were obtained, but by estimate from Figs. 4 and 5 it probably fell below 7.00. Following a common bile duct exploration and cholecystectomy, as this patient was moved to the recovery room, the blood pressure dropped to 80/60. This response was quite incompatible with the amount of blood lost and replaced during the operative procedure.

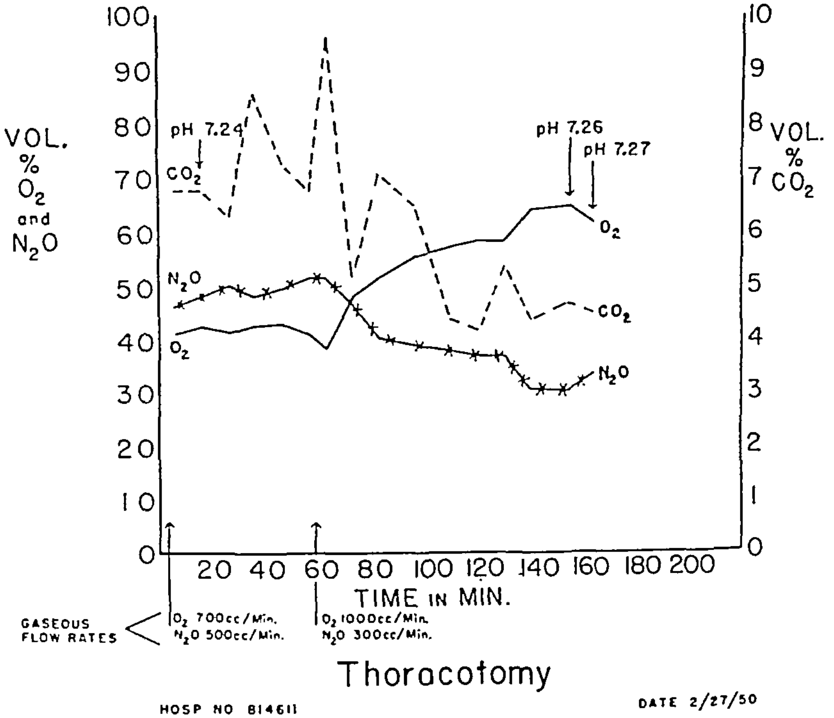

Fig. 10.—This illustrates another mass spectrometer tracing of a patient with a thoracotomy.

Hypotension persisted for 7 days, except when relieved periodically by ephedrine and neo-synephrine administration. During this period there was a diminished urine output, a rise in blood urea nitrogen to 77 mg. per cent on the fourth postoperative day, and a marked electrolytic imbalance. Serial eosinophil counts showed no diminution following an injection of epinephrine on the ninth postoperative day. On the seventh postoperative day the blood pressure rose to 110/60 and afterward stabilized above 100/70 as the patient gradually convalesced.

Table I presents a summary of the highest carbon dioxide concentrations recorded by the mass spectrometer for each case. The average was 7 per cent or approximately double the normal value. This suggests that at some time in these operative procedures the average case had an alveolar carbon dioxide con-

TABLE I. LARGEST CO_2 VALUES RECORDED BY MASS SPECTROMETER DURING THIRTY-FOUR OPERATIONS

PROCEDURE	ANESTHESIA	TOTAL NUMBER CASES	NUMBER OF CASES					AVERAGE LARGEST CO_2 CONCENTRATIONS
			LESS THAN 5% CO_2	5 TO 6% CO_2	6.5 TO 8% CO_2	8 TO 10% CO_2	10% CO_2 OR GREATER	
Pneumonectomies	Ether	1	–	–	–	–	1	10.0
Lobectomies	Pentothal, curare, N_2O	2	1	–	–	–	1	7.5
Miscellaneous Thoracotomies	Ether	1	–	1	–	–	–	5.2
	Pentothal, curare, N_2O	12	4	1	3	3	1	6.7
Laparotomies	Ether	10	5	2	3	–	–	5.6
	Pentothal, curare, N_2O	5	1	1	3	–	1	9.3
Miscellaneous	Ether	1	1	–	–	–	–	4.4
	Pentothal, curare, N_2O	2	–	1	–	1	–	7.0
Total	Ether	13	6	3	3	0	1	5.6
	Pentothal, curare, N_2O	21	6	3	6	4	3	7.7
	Composite	34	12	6	9	4	4	7.0

centration of about 10 per cent and that this situation was associated with an arterial pH of approximately 7.20.

DISCUSSION

The correlation data shown in Figs. 4 and 5 reveal a definite pattern between the alveolar carbon dioxide samples as estimated by the Henderson-Hasselbalch equation and those values recorded by the mass spectrometer. The latter are uniformly lower. The high reproducibility between the mass spectrometer and chemical gas analyses, earlier referred to, confirm the likelihood that the gas sampled by the mass spectrometer did not represent true alveolar gas. It is difficult to deliver a true alveolar sample to the analyzer without interfering with anesthetic techniques. It was necessary therefore to standardize the instrument and the involved setup by biologic testing and extrapolation from this for clinical material. The results shown in Fig. 5 indicate that the normal carbon dioxide value was 3 to 3.5 per cent.

In so far as the acid base balance was concerned, this method is only applicable in assaying an uncompensated respiratory acidosis or alkalosis in which the alteration of pH is due solely to either an increase or decrease in carbon dioxide tension as the result of change in alveolar carbon dioxide concentrations. In a metabolic type of acidosis with the removal of fixed base or with the addition of fixed acid, the pH diminution is not due to an increased alveolar carbon dioxide tension, and the acidosis assuredly would not be revealable by the mass spectrometer. Beecher's concept[1] of a metabolic acidosis with an accumulation of fixed acid secondary to prolonged hypercapnia therefore introduces another unknown capable of altering the pH-CO_2 relationship. This situation with several vectors is only partially solvable by data from the mass spectrometer.

A limitation of the mass spectrometer-pH correlation data appears in the states of compensated respiratory acidosis or alkalosis. Here the fixed base of the body has been adjusted in order to compensate for the respiratory maladjustment. For example, in an emphysematous individual if one were to judge from only an elevated alveolar carbon dioxide concentration, it would seem that the patient was in a state of acidosis due to carbon dioxide accumulation. However, pH determinations might well show normal values because of the retention of base by the kidney so as to effectively neutralize the acidotic tendency. An example of this type of error is seen in Fig. 7, the chart of a case of tetralogy of Fallot on whom a Blalock-Taussig anastomosis was performed. It will be noted that the carbon dioxide values were consistently under 3 per cent. Under ordinary circumstances one would assume this to be due to overventilation of the patient by the anesthetist, leading to a respiratory alkalosis. However, pH determinations performed when the mass spectrometer reading was 2 per cent showed a slight acidosis. An attempt to raise the alveolar carbon dioxide concentration by hypoventilation would have aggravated the acidosis. The explanation hinges about the customary respiratory alkalosis these individuals carry secondary to chronic hyperventilation as described and analyzed by Bing and associates.[10] Here the kidney compensates for the diminished alveolar carbon dioxide tension by excreting base so as to hold the pH at 7.40. Therefore, in the case illustrated, when the mass spectrometer recorded a level of 3 per cent, which is normal for most cases, the child would undoubtedly have shown a pH depression, had an analysis been performed at that time, because the amount of base available would be insufficient to neutralize the accumulated carbon dioxide. Fortunately this discrepancy between pH-CO_2 values due to preoperative compensation can be corrected by drawing an arterial sample sometime preceding surgery and analyzing it for total carbon dioxide content and pH. Consistently low carbon dioxide records in association with diminished pH values have been obtained in three cases of this type. However, in all of these cases the carbon dioxide analyses were also complicated by the fact that comparable intratracheal samples could not be obtained due to impedance of the airway by the sampling tube. Accordingly these cases have not been included in the pH-CO_2 correlation curve (Fig. 5).

Mass spectrometer determinations made during ordinary operative procedures are valid since the compensating mechanism of base excretion or retention by the kidney lags. When one sees, therefore, a rise or fall of carbon dioxide concentration during an operation it is virtually inconceivable that kidney compensating mechanisms account for this but rather it represents an actual shift of acid-base balance.

A rise in blood pressure has been the common sign accepted by anesthetists as signaling the presence of carbon dioxide excess. During any major surgical procedure so many variables are present to interfere with the blood pressure as to make it extremely unreliable as a diagnostic sign of hypercapnia. This has been substantiated by the carbon dioxide analyses. In only a few instances was there a rise in blood pressure coincident with carbon dioxide elevation.

While carbon dioxide excess in the ranges observed is normally a marked respiratory stimulant, the anesthetic agents so effectively interfered with the function of the respiratory center that an increase in respiratory rate or volume was seldom noticed in conjunction with high carbon dioxide levels.

The toxic effects of carbon dioxide in asphyxia are well documented.[11] The depressant effect of high inhaled carbon dioxide concentrations on the respiratory center are also well known.[12] The narcotizing effect of carbon dioxide inhalation has been demonstrated with its use as an anesthetic agent.[13] Waters[14] described one postanesthetic death which he stated was most likely the result of hypercapnia. Indeed it seems a reasonable hypothesis that some of the unexplained grave operative sequelae, including cardiac standstill, are connected with this problem.

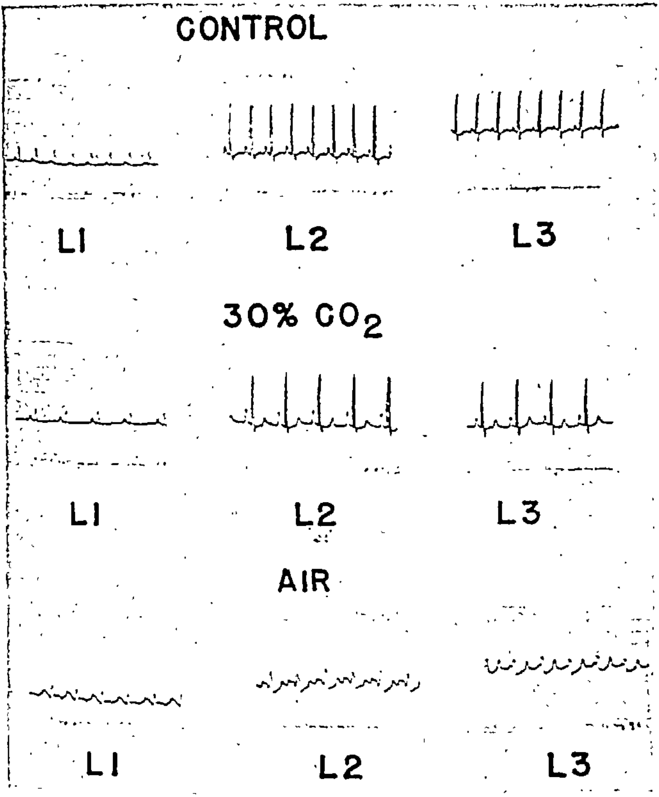

FIG. 11.—Electrocardiographic tracings of anesthetized dogs taken before, during, and after breathing 30 per cent CO_2/O_2 mixtures.

The postoperative complications in the instance in which the carbon dioxide level reached 17.3 per cent introduce interesting speculative possibilities in association with certain laboratory investigations. It has been demonstrated in the dog that alveolar carbon dioxide concentrations above 15 per cent produce depression of adrenal function as evidenced by the absence of an eosinopenia following the injection of epinephrine.[15] The duration of this effect after cessation of the hypercapnia awaits further studies. Depressed adrenal function conceivably could account for most of the following postoperative complications observed in this patient: hypotension, diminished serum sodium, depressed carbon dioxide combining power, depressed kidney function as evidenced by diminished urinary output and rise in blood urea nitrogen and creatinine. Another factor which must be taken into account is that the patient had markedly abnormal liver function tests both pre- and postoperatively. Seevers and Orth have shown that inhalation of high carbon dioxide concentrations probably produces injury to the liver.[16, 17] The complications observed in this case, including the low blood pressure, would also be compatible with liver damage. It is quite likely that carbon dioxide accumulation during surgery may have been the trigger mechanism responsible for the depression of one or both of these vital organs and may have provoked the serious sequelae outlined.

Studies are underway in this laboratory evaluating the toxicity of high concentrations of carbon dioxide in the inspired air of anesthetized experimental animals. So far these studies have indicated changes along the following lines: (1) electrocardiographic evidences of myocardial damage, (2) decreased tolerance to pentothal and Nembutal, (3) marked arterial blood pH depressions.

Fig. 11 shows a set of electrocardiographic tracings during the course of an experiment. This record is typical of a number of others that have been obtained with the same procedure. The upper three tracings are the control records taken following pentothal anesthesia. The middle set were taken while the animal was breathing 30 per cent carbon dioxide and 70 per cent oxygen, and the last group represents a time interval ten minutes after the animal had been taken off the carbon dioxide mixture and returned to breathing room air. In the latter tracing there is a marked depression of the ST segment suggestive of myocardial anoxia. That a marked hypotension occurs following the cessation of inhalation of high concentrations of carbon dioxide has been shown by other investigators.[18] Whether the hypotension causes the myocardial changes evidenced by the electrocardiographic records or whether the reverse situation occurs has not been ascertained.

Another phase of these studies was the demonstration of decreased tolerance to pentothal and Nembutal. A marked blood pressure fall and bradycardia were noted after administration of the drugs following a period of inhaling mixtures of high carbon dioxide content. After a period of breathing 30 per cent carbon dioxide and 70 per cent oxygen three out of ten dogs died suddenly subsequent to the administration of pentothal or Nembutal doses ordinarily readily tolerated by normal dogs. Beecher and Moyer have also demonstrated a decreased tolerance to barbiturates in the presence of respiratory acidosis.[19]

Inhalation of 30 per cent carbon dioxide caused a pH depression as low as 6.61 in some of the dogs.[20] This is considerably under the level of 6.80 to 7.00 commonly acknowledged in standard textbooks of physiology to be the lower limit compatible with life. Surprising as it is that these dogs survived, it is perhaps no more important than the warning that such high alveolar carbon dioxide concentrations produce such critical arterial pH values. It is to be emphasized that these were acute experiments and no attempt was made to examine the postacidotic sequelae. Furthermore the tolerance of healthy mongrel dogs to acidosis is likely to be disproportionately more elastic than for patients assaulted by chronic disease and the stresses of both anesthesia and major surgery.

SUMMARY

A portable mass spectrometer functioning as a continuously recording gas analyzer is described. The clinical adaptation of the instrument has been noted, with reference to its future in the operating room as an aid to the anesthetist in ascertaining the carbon dioxide concentration in expired air. Graphs are shown of the results with five typical cases. These graphs also show concentrations of oxygen and anesthetic gas in the sample.

The correlation of the carbon dioxide concentration and arterial blood pH are shown both in experimental animals and patients. These results indicate a reasonable agreement between two methods of analysis.

This instrument has tested quantitatively the concentration of exhaled gases during thirty-four major operative procedures, including many transthoracic procedures. It is demonstrated that on the average a level of 6.8 per cent carbon dioxide was reached at one time or another during most of those cases. This corresponds to an arterial blood pH of 7.20 and an alveolar carbon dioxide concentration of approximately 10 per cent.

The postoperative complications in one case in which the carbon dioxide level reached 17.3 per cent are reviewed.

Results are reported from carbon dioxide toxicity experiments carried out on experimental animals.

The authors gratefully acknowledge the technical assistance of Mr. Howard Demorest and Miss Margaret Murray.

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THE SURGICAL TREATMENT OF GIANT EMPHYSEMATOUS BLEBS AND PULMONARY TENSION CYSTS

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In 1925 Koontz[1] reported the first case of emphysematous blebs in the American literature. Shortly thereafter, Miller[2] attempted to clarify the differential pathology between blebs and bullae, and was further of the opinion that these localized abnormalities were always associated with a generalized emphysema. Miller described a bleb as a subpleural collection of air caused by rupture of pulmonary alveoli immediately beneath the pleura allowing the air to escape into the pleura forming a thin-walled bladder-like prominence outside the lung itself. He defined a bulla as a vesicular emphysema situated within the lung, and though it often projected beyond the surface of the lung, it was covered by an intact pleura. In the subsequent literature many synonyms have been used: pneumatocele, cystic emphysema, air cyst, bullous emphysema, emphysematous blebs, and vanishing lung; all of these terms conform to Miller's original concept of subpleural blebs.

Study of our own surgical material indicates that we removed blebs only, but for practical purposes there does not seem to be great merit in attempting to distinguish between blebs and bullae. In some cases, we have removed localized blebs from lungs which grossly, at least, showed no evidence of emphysema. Extended inquiry into the pathogenesis of pulmonary emphysema is not germane to this presentation. Differentiation, however, should be made between emphysematous blebs and intrapulmonary cysts. Much of the literature is confusing. In our opinion, pulmonary cysts are congenital in origin, have a definite fibrous tissue wall, and are lined by epithelium. Emphysematous blebs are acquired, perhaps very early in life and have either no lining or at most have an alveolar type of flattened epithelium.

Why these lesions develop is not at once apparent nor can it be determined why all patients with emphysema do not develop large air cysts. Suffice it to say that the end result in many patients is a great decrease in pulmonary function with symptoms ranging from mild dyspnea to severe incapacitation. Definite therapy therefore becomes necessary.

METHODS OF THERAPY

No one familiar with this disease questions the necessity for treatment of individuals presenting severely incapacitating or life-threatening symptoms from bullous emphysema. The therapeutic approach has been the subject of

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considerable controversy and authoritative sources recommend many measures varying from a "conservative" regime of observation to extensive excisional surgery. Spontaneous disappearance of an emphysematous cyst without active treatment of any kind has been reported.[3, 4, 5] This phenomenon has been explained on the basis of rupture, absorption of air, and gradual expansion of the previously compressed lung. These remarkable cures have been reported in infants under two years of age for the most part but, unfortunately, are the exception. Needle aspirations of the air-containing sac has likewise resulted in complete clearing.[4, 6, 7, 8] The danger, however, of sudden exodus by needle rupture of a cyst has long been recognized[9, 10, 11] and such a procedure should never be attempted without facilities for immediate thoracotomy. In line with this same therapeutic approach, the injection of Lipiodol and caustics has been advanced. King and Harris[12] reported the successful treatment of a congenital lung cyst by intracavitary injections of iodized oil with subsequent closure of the bronchial communications but at the same time (1937) predicted that excisional surgery would ultimately be the most effective treatment. Hennell[13] had a similar experience with Lipiodol. Silver nitrate cauterization of a cyst wall following open drainage was reported by Pierson,[14] in 1935, and again two years later by Field and Rosenberg.[15] In 1928, Eloesser[16] felt quite strongly that only infected cysts should be treated and these he drained by his flap technique following later with a plastic procedure to close the opening in the chest wall. In 1931, Eloesser[17] added subsequent lobectomy with closure of the fistula to his primary drainage operation. Anderson,[18] in 1937, likewise felt that drainage of infected cysts was the preferred treatment. Brown and Brock,[19] in 1942, advocated the endocutaneous flap procedure for the treatment of a large cyst and in their report described the technique of exteriorization of the cyst wall. These early therapeutic endeavors were during the period when thoractomy was hazardous and represented a compromise with surgical principles of intrathoracic exploration as we know them today. Such historical attempts are for the most part discarded procedures at the present time.

Nissen,[20] in 1945, advocated thoracotomy, direct opening of the cyst, and repair by a plication-inversion suture technique. This procedure was performed in two cases with ultimate success, although there was delay of several weeks in the re-expansion of the affected lung. Head and Avery[21] presented the technique of decompression of an emphysematous bleb by intracavitary suction identical with Monaldi drainage and provided an excellent approach to the problem. In their series of eight cases good results followed this minor procedure under local anesthesia. They emphasized the applicability of suction therapy to the patient whose vital reserve is dangerously reduced because of high intracavitary pressure. We can best stress, however, that at thoracotomy these pressures are removed as soon as the chest is opened and the patient's condition routinely and immediately improves to essentially a normal status as far as oxygenation is concerned. Head and Avery believe the uniform absence of pleural adhesions in their cases was possibly a cooperative factor in the development of the blebs. This drainage method also was advocated by Lloyd[7] and may be well suited to patients with but a single giant bleb. It should be of little value, however, in the presence of multiple blebs which was the situation in many of our cases. Unfortunately, the roentgen examination frequently cannot tell us whether the blebs are single or multiple.

During the past ten years there has been an ever increasing number of essayists strongly favoring excisional surgery in the approach to this problem. Brock,[22] Ravitch and Hardy,[23] and Naclerio and Langer[24] reported the largest number of cases treated by resection but many other surgeons have been sponsors of this approach.[10, 25-28, 29-31] Burnett[32] and associates stressed the importance of careful selection of surgical cases and were most optimistic in those with well localized disease. Clagett[33] favored resection with utilization of segmental removal in suitable cases.

DIAGNOSIS AND SELECTION OF CASES

In the past three years, we have operated upon fourteen patients with giant emphysematous blebs by lobectomy, segmental resection, or local excision of the tissue involved. The cases subjected to surgery have been carefully selected. The importance of painstaking evaluation of the individual surgical candidate cannot be overemphasized. As is true in all types of surgical procedures, the best results are obtained in the younger age group although such fact does not preclude surgery in the older individuals if legitimate indications exist. The extremes in our cases were three months and sixty years of age. All of the patients presented definite symptomatology referrable to the chest, the presenting complaint unanimously being increasing dyspnea. All, with the exception of the infants, were faced with an immediate serious occupational handicap.

The two most important considerations are the symptomatology and the roentgen appearance. The prospective surgical patient usually presents the history of increasing dyspnea, pain in the chest, and frequent respiratory infections. He may also complain of slight dysphagia, cough, a feeling of pressure in the chest, and general fatigue. Physical examination in general reveals diminution of excursion over the involved area with decreased breath sounds. The roentgen appearance is essential in the diagnosis and is the most important single finding in the localization of the lesions to one or both lungs. Bilateral disease is not a contraindication to surgery but a unilateral lesion is much more encouraging. The pathologic area appears black and lacking in lung elements. In many instances the roentgen film gives the impression of a localized pneumothorax, the increased transparency of the lung being due to actual loss of vascular markings. The surrounding lung appears compressed and in those areas the vascular markings are increased. The lesions are for the most part located in the basilar areas although apical lesions of this type are common. If serial roentgenograms are available there is usually evidence of progression in size. Bronchoscopic examination reveals twisting and distortion of the bronchial orifices so that the normal relationship is disturbed. Lipiodol bronchograms are routinely produced to rule out the possibility of associated bronchiectasis. Bronchography is of further aid in determining the amount of normal lung tissue that can be depended upon for re-expansion as well as to forecast in advance of surgery the type of resection which will be required. Bronchospirometric readings and vital capacity studies were not performed in our surgical cases.

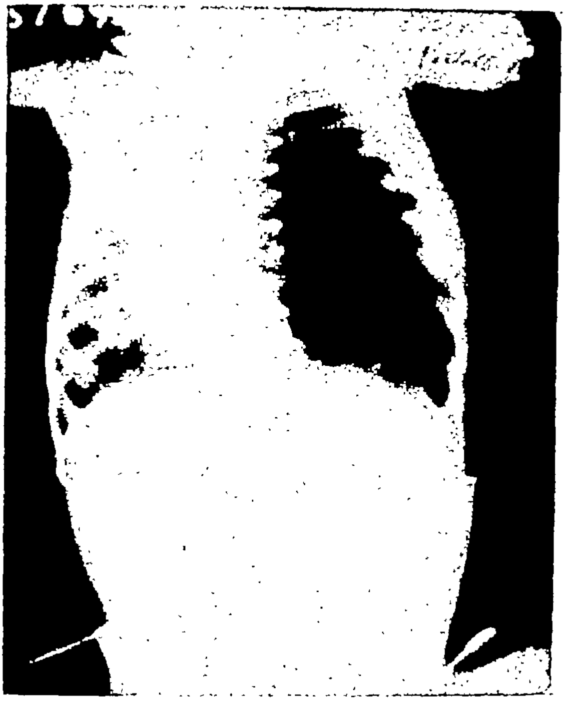


Fig. 1 (Case 1).—Roentgenogram taken immediately before left thoracotomy.

CASE REPORTS

CASE 1 (P. B.).—This 3-month-old infant girl was brought to her family physician on Aug. 5, 1948. For the preceding two months the parents had noted increased respirations and right-sided heartbeat. Roentgen examination revealed a displacement of the mediastinum and heart far to the right and a large emphysematous area occupying the entire left chest (Fig. 1). The patient was hospitalized and needle aspiration and intracavitary drainage were unsuccessful. Left thoracotomy was performed on Aug. 26, 1948, and immediately, when the pleura was opened, a giant emphysematous bleb eviscerated through the wound and was seen to occupy the entire lower lobe exclusive of the superior segment (Fig. 2). As soon as the chest was opened, the patient's condition improved. The left upper lobe was atelectatic, displaced in the upper posterior mediastinum and to the right of the vertebrae. An anatomic resection of the basal segment of the left lower lobe was performed. The postoperative course was satisfactory except for the development of an osteomyelitis of a rib end at the site of the drainage tube. This healed per primam after local resection. A ten-month follow-up showed a normal appearing chest (Fig. 3). Today the child is clinically normal.

CASE 2 (H. W.).—This second case demonstrates the value of early removal of emphysematous blebs in anticipation of the possibility of secondary infection and abscess formation. This 48-year-old man was first seen by us on July 9, 1948, with a history of having an "air pocket" in his right lung since 1945. Periodic respiratory infections had occurred for the past three years and on this hospital admission he complained of general malaise, cough, and low-grade fever. Roentgen examination of the chest revealed a large emphysematous bleb occupying the right apex with an associated pneumonitis (Fig. 4). Comparison with radiographs made in 1945 showed definite evidence of progression. Bronchoscopic drainage relieved the cough and pyrexia and the patient elected to postpone surgery. One week later a fluid level developed within the emphysematous area (Fig. 5) and the patient submitted to operation. At thoracotomy a large emphysematous bleb which occupied the entire right apex was removed. At its upper and lower lobe attachments it was

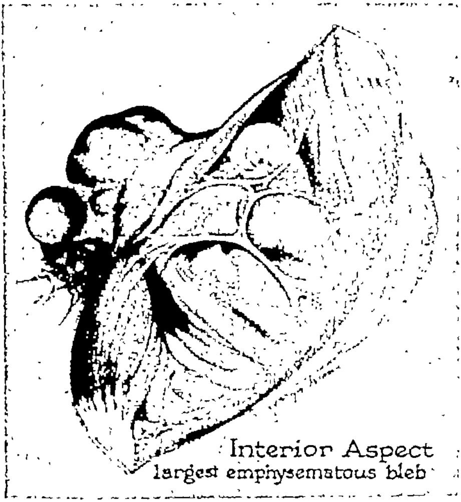


Fig. 2 (Case 1).—Schematic drawing of left lower lobe bleb occupying basal segments.

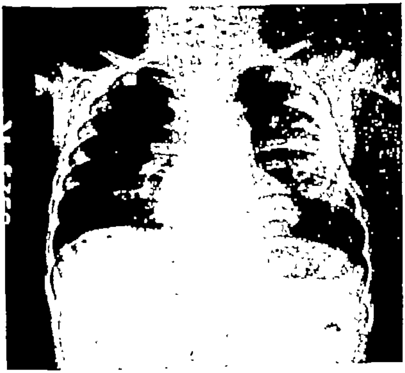


Fig. 3 (Case 1).—Roentgenogram taken ten months following resection of basal segments of left lower lobe for large emphysematous cyst.

mothorax. However, there are generally some differential points which too often are found only after reviewing the roentgenograms. In the presence of a pneumothorax the elastic lung will generally contract about the hilum and will appear as a globular shadow while with a "vanishing lung" the hilar shadow is generally elongated and areas of compressed lung may be seen in the apex of the thorax or over the diaphragm. The widening of the intercostal spaces produced by large cysts may be apparent (Fig. 3), as opposed to the narrowing of the interspaces that is found in chronic pneumothorax.[9]

TREATMENT

The therapy of cystic lesions has been varied. Treatment based on external compression of the lesion has failed.[5] External drainage has only been partially successful. In reviewing the literature it seems evident that some lesions responded well to external drainage by intracavitary suction (Monaldi),[8] or by an endocutaneous flap using Eloesser's method.[3] However, such methods are not always effective as indicated by the reports of prolonged open drainage of cysts without spontaneous closure.[11] The lesion has often been mistaken for thoracic empyema preoperatively and generally these cysts have required open drainage.

It is paradoxical that lesions appearing to be of similar nature respond differently to similar treatment. It seems likely that a different pathogenesis exists, although the lesions seem to be clinically identical. It is possible that the difference lies in the character of the lining membrane; those cysts lined by respiratory epithelium resisting closure, and those lined by alveolar and fibrous tissue closing promptly when the balloon effect is eliminated and the walls are apposed. Throughout the case reports in the literature there is consistent difficulty in distinguishing the cysts lined by epithelium from those without epithelial lining before histologic study of the tissue. Excision of the lobe or lung containing the cyst has been effective in treatment[4, 7, 15, 18, 19] but has the objection of sacrificing nondiseased lung tissue in many instances. Closure of the fistula followed by suture of the opposing walls of the cyst has recently been advocated by Naclerio and Langer.[17] This method is advantageous in sacrificing the minimal amount of lung tissue, but in cysts lined by epithelium the opposed surfaces might fail to unite. Chemical cauterization of the surface of the cyst in order to sclerose the wall and close the bronchiolar orifices has been used successfully[6] but is an unpredictable method.

In view of our inability to differentiate between epithelialized and nonepithelialized balloon cysts in the lung, we have directed our treatment toward excising the wall of the cyst, closing the bronchiolar orifices, sacrificing only that lung parenchyma adjacent to the cyst, and re-expanding the lung by temporary suction drainage postoperatively. The involved lobe or lung has not been removed in any instance, since it seemed a needless sacrifice of normally functioning pulmonary tissue. In those instances of multiple bilateral large cysts, as in the cases cited by Head and Avery[8] intracavitary suction drainage may be indicated rather than thoracotomy and excision of the cyst wall.

CASE REPORTS

CASE 1.—A 25-year-old white woman had been free of symptoms until six weeks preceding admission to the hospital. At that time she had been seen by her physician for treatment of an upper respiratory infection. She had no other respiratory symptoms but had persistently been below her expected weight and had chronic fatigue. There was no history of dyspnea. There were signs of a left tension pneumothorax. She was observed at weekly intervals and as there was no evidence of re-expansion of the lung she was referred to this hospital for treatment.

The patient appeared chronically ill, weight was 95 pounds. The significant physical findings were those of a left tension pneumothronx (Fig. 1, *A*). A left thoracentesis was done; 5,000 c.c. of air were removed without change of pressure or expansion of the lung. Following this, air escaped into the pleural space and delineated the cyst margin, (Fig. 1, *B*). On May 17, 1948, a left thoracotomy was performed and a large cyst found which filled the hemithorax. It arose from the anterior segment of the left upper lobe. When the cyst was opened it promptly deflated and multiple small bronchiolar orifices were evident in the trabeculated base. The surrounding lung parenchyma promptly inflated. The cyst was excised and suction drainage of the pleural space was established.

The patient had an uneventful postoperative course with re expansion of the lung, and was discharged from the hospital on the fourteenth postoperative day. Microscopic examination of the excised cyst wall showed only connective tissue. Six months after operation the patient had gained twenty pounds, was asymptomatic, and the lung was well expanded (Fig. 1, *C*). She had no fatigue with normal activity.

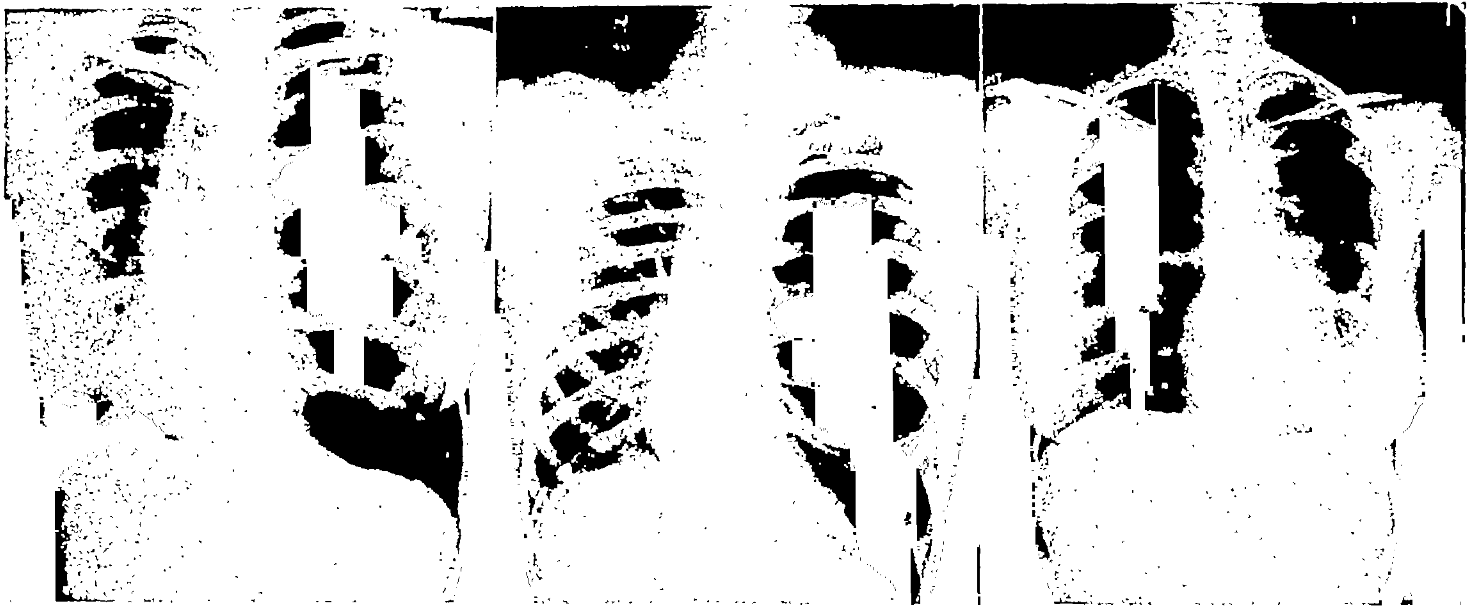
Comment.—It is hardly conceivable that the cyst would reach a size sufficient to compress both the homolateral lung and ipsilateral lung without giving severe dyspnea. A rapid reduction of lung volume to this extent would certainly produce symptoms. One can only speculate on the likelihood of chronic oxygen want preceding obliteration of the lesion due to the gross diminution of functioning pulmonary tissue. Postoperatively the loss of fatigue, the gain in weight, and general sense of great improvement would suggest the possibility of the correction of a chronic anoxia.

CASE 2.—A 16-year-old white boy had been free of symptoms until three years preceding admission, when he first noticed shortness of breath with exercise. One year preceding admission dyspnea had been particularly marked when playing basketball. Six months later a survey chest roentgenogram was interpreted as showing a left pneumothorax. This had not changed significantly during the six months before admission to the hospital. Studies for the presence of tuberculosis were negative.

The only significant findings on admission were limited to the left hemithorax. There was widening of the interspaces on the left with increase in the size of the entire hemithorax. The findings of a large pneumothorax were present on the left, the mediastinum being displaced to the right (Fig. 2, *A* and *B*).

A left thoracentesis was performed and a gas specimen obtained from the cyst, which contained 6 per cent carbon dioxide and 8.9 per cent oxygen; the intracavitary pressure was +4 to −4 cm. of water.

On Dec. 10, 1948, thoracotomy was performed and a large cyst was found to occupy the left hemithorax. After opening the cyst two bronchiolar orifices could be seen at the trabeculated base. The origin of the cyst was from the left upper lobe. The bronchiolar openings were closed, the roof removed from the cyst, but the portion adherent to the lung parenchyma was left intact. The upper lobe promptly expanded. Adhesions binding the lower lobe inferiorly and medially were divided, which was followed by prompt expansion of the entire lung, although it did not completely fill the hemithorax. The chest was closed about a catheter for suction drainage. Histologic study of the excised cyst wall showed only connective tissue.



A. B. C.

Fig. 1.—*A*, Roentgenogram of Case 1 showing what appears to be a left pneumothorax with displacement of the heart and mediastinum into the right hemithorax.

B, Roentgenogram of Case 1 after aspiration of cyst. Gas had escaped into left pleural space and the thin cyst wall is delineated inferiorly. The collapsed lower lobe is now visible.

C, Six months postoperatively there is moderate pleural thickening in the left hemithorax with mediastinal shift to the left.

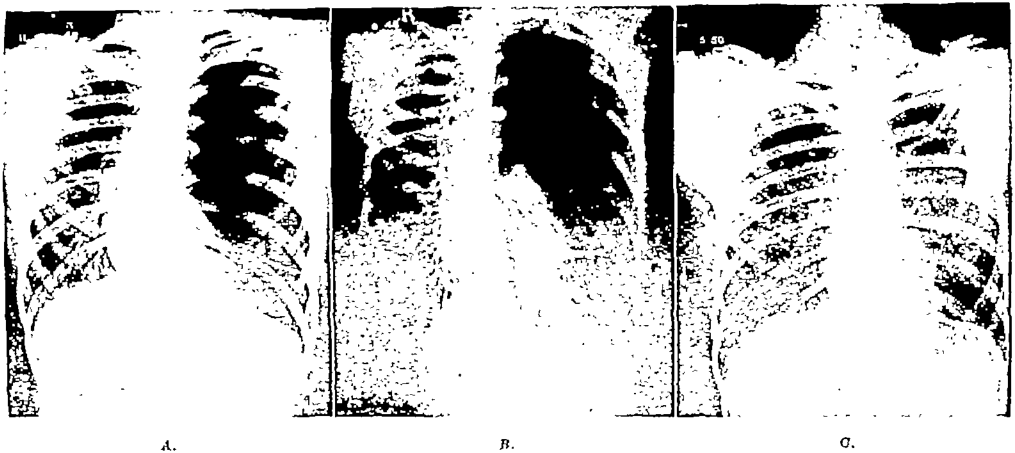


Fig. 2.—*A*, Roentgenogram of Case 2. Note widening of interspaces of left hemithorax and compression of lung medially. *B*, Bronchogram of Case 2. Note crowding of all bronchial subdivisions. An artificial pneumothorax outlines the cyst wall. *C*, Roentgenogram one year postoperatively. The widening of the interspace on the left has persisted.

Postoperatively a small apical pneumothorax persisted. The drainage tube was removed on the fifth postoperative day. Development of an apical empyema required open drainage on the thirtieth postoperative day. The cavity was then spontaneously obliterated and the patient was discharged fifty-seven days after operation. He was free of symptoms one year later (Fig. 2, *C*).

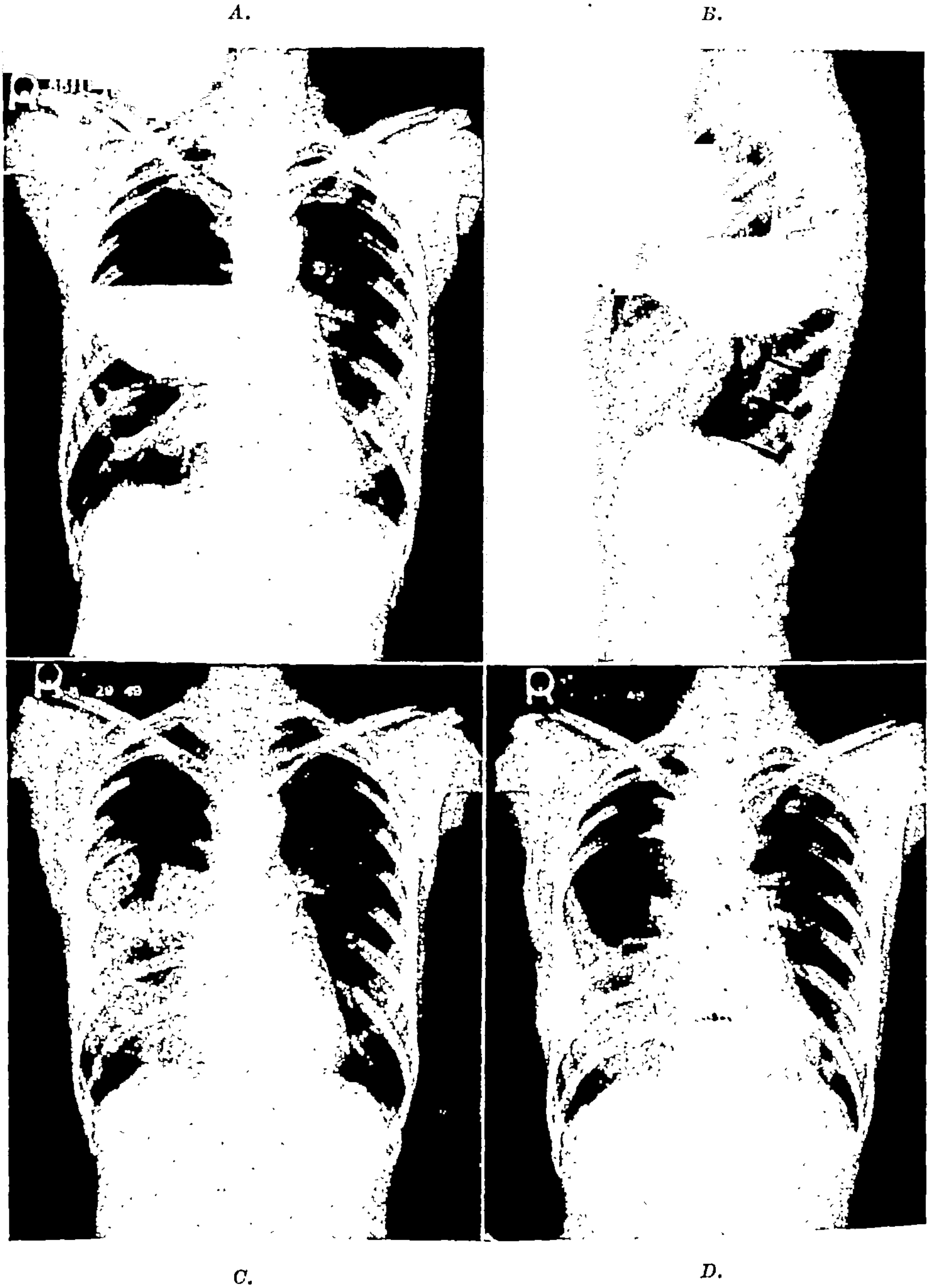


Fig. 3.—*A*, Anteroposterior roentgenogram of Case 3 on admission.

B, Lateral roentgenogram of Case 3 on admission.

C, Roentgenogram of Case 3 nine weeks following adequate dependent drainage. The size of the space has not decreased appreciably.

D, Roentgenogram of Case 3 four weeks following excision of the cyst. A small apical pneumothorax persisted but subsequently the lung re-expanded spontaneously.

Comment.—The presence of dyspnea on activity over a period of years suggests that this cyst had been present for a long time. The persistence of an apical pneumothorax followed by an infection of the space postoperatively indicates that a bronchiolar orifice was left unclosed at operation. In this instance a portion of the lining of the cyst wall was left intact which may have influenced the occurrence of infection.

CASE 3.—A 33-year-old white woman was admitted to the hospital with a draining sinus on the posterior surface of the right hemithorax. A thoracotomy had been done in this hospital June 23, 1940, and a large collection of pus was drained from the right hemithorax, with a diagnosis of infected giant lung cyst (Fig. 3, *A* and *B*). After discharge the large cavity had not decreased in size and a bronchopleural fistula had remained patent, with persistent profuse drainage.

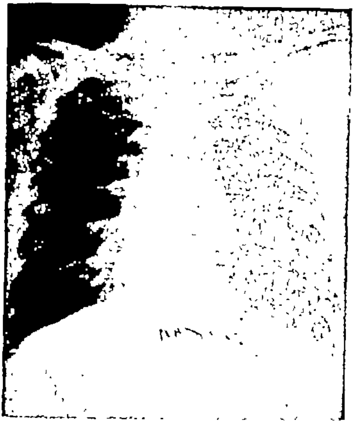


Fig. 4.—Roentgenogram of Case 1 on admission. There is a left pneumothorax of moderate size. The collapsed lower lobe is seen as a hilar mass, and upper lobe lung markings are visible.

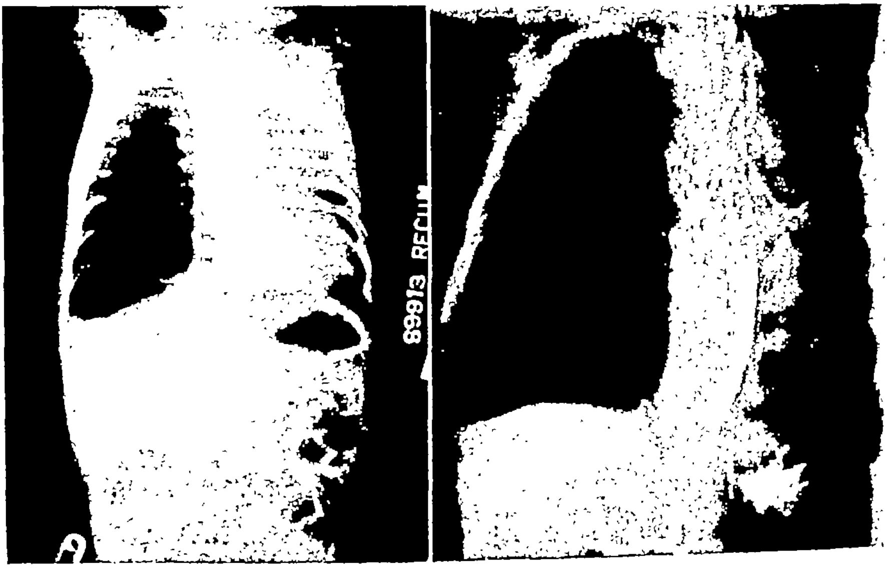
On the second admission the significant findings were limited to the right hemithorax. There was a granulating drainage tract through the thoracic wall at the area of the angle of the eighth rib. The tract entered a spacious cavity that appeared to be lined with epithelium (Fig. 3, *C*). The depth of the cavity was trabeculated and several fistulas were evident. There was a copious amount of thick pus within the cavity.

On Aug. 17, 1940, the sinus tract was widely opened to afford access to the cavity for cleansing; after a few days of treatment the secretion was greatly reduced. On Sept. 9, 1940, a thoracotomy was performed. The sinus was excised. A large cystic space was found filling the entire superior portion of the right pleural cavity. The space was opened widely, the wall of the cyst was excised, and the base was found to arise from the posterior segment of the right upper lobe. The base was excised and the bronchiolar orifices closed. The adhesions of the lung were then divided and the lung expanded promptly to fill the entire pleural space except for a small area at the apex. Catheter drainage of the apical area of the space was established and the wound closed by using a muscle flap from the trapezius and latissimus dorsi to close the defect incurred in the chest wall produced by extension of the fistulous tract. Histologic study of the cyst wall showed bronchiolar epithelium.

The postoperative course was uneventful and the patient was discharged on the seventeenth postoperative day with the wound well healed (Fig. 3, *D*). In a follow-up examination three months following operation she was free of symptoms; the lung was normally expanded.

Comment.—This large cyst was drained externally even though recognized as an infected giant cyst of the lung preoperatively because of concomitant pneumonitis. After drainage there was no tendency for the space to obliterate. Excision of the lining membrane of the cyst with closure of the bronchiolar orifices was required before the lung would re-expand. Only a small amount of lung tissue was sacrificed.

CASE 4.—A 61-year-old white man had a sudden attack of severe dyspnea three months preceding admission. He had an upper respiratory infection with paroxysms of coughing preceding the onset of dyspnea. His local physician found a left pneumothorax. Repeated aspirations of the chest and prolonged bed rest did not influence the collapsed lung. He was referred for hospital treatment because of the persistence of severe dyspnea and a left pneumothorax.



A. *B.*

Fig. 5.—*A*, Roentgenogram of Case 5 on admission. The heart is displaced to the left. The right lung appears to be compressed.

B, Bronchogram of Case 5. Note compression of the entire right lung along the mediastinum with shift of all mediastinal structures to the left.

The findings of significance were those of a left pneumothorax with complete collapse of the left lower lobe and partial expansion of the left upper lobe which was suspended from the apical thorax by adhesions (Fig. 4). Studies for tuberculosis were negative.

Thoracotomy was performed on Dec. 23, 1949. A large cyst arose from the anterior segment of the left upper lobe. Unfortunately the cyst was entered as the parietal pleura was incised and no definite point of spontaneous leakage was determined. A small trabeculated base with multiple bronchiolar orifices was found in the anterior segment of the left upper lobe. When the entire wall was excised and the orifices closed the entire lung promptly re-expanded. The chest was closed about a catheter drain for suction. Histologic study of the wall showed only connective and granulation tissue. The patient had an uneventful postoperative course, the lung expanded, and he was discharged from the hospital on the eighth postoperative day. He has been free of symptoms since discharge.

Comment.—This illustrates a common complication of blebs and bullae. It is surprising that clinical evidence of infection was not superimposed in view of the prolonged leakage through the cyst wall. The absence of any symptoms preceding an upper respiratory infection suggests that this cystic lesion may have been acquired quickly and was of short duration.

CASE 5.—A 9-week-old boy had respiratory difficulty since birth. A week preceding admission the infant had increasing air hunger manifest by rapid respiration and cyanosis on exertion. Examination gave evidence of a right tension pneumothorax. Roentgenographically there was gross mediastinal displacement to the left, with only a few lung markings on the right side (Fig. 5, *A*). A bronchogram showed compression of the entire right lung along the mediastinum (Fig. 5, *B*).

Operation was performed on Feb. 10, 1950, and a large multiloculated cyst of the right lower lobe was found. It was necessary to sacrifice portions of the posterior and lateral basal segments of the lobe due to the attenuation of lung parenchyma in those areas. The cyst wall was excised. During the closure of the bronchiolar orifices complete obstruction of the airway developed, the infant became cyanotic, and cardiac arrest occurred. A tracheotomy was started but before it was completed the airway obstruction was relieved, possibly by the hyperextension of the neck. Manual cardiac massage had been maintained and the heart promptly regained its normal rhythm. The chest was quickly closed about a catheter drain for suction and no further bronchiolar closure was accomplished, but it was felt the main orifices had been closed. Histologic study of the cyst wall showed the lining to be composed of respiratory epithelium and connective tissue. A persistent air leak occurred for nine days postoperatively. This sealed spontaneously and the infant was discharged on the twenty-first postoperative day with the lung expanded except for a small residual basal air-pocket. Twenty-three days following discharge he was re-admitted with findings of a right tension pneumothorax. Suction drainage of the pleural space was established, the lung promptly re-expanded. Drainage was discontinued after seventy-two hours, the infant was discharged fourteen days after admission with findings of a completely re-expanded lung.

Comment.—This patient illustrates the early age at which these lesions occur. The histologic finding of both respiratory epithelium and connective tissue in the lining of the cyst suggests that the rapid expansion of the cyst after birth may have ruptured the epithelial lining in the ballooning process.

The occurrence of a tension pneumothorax following discharge suggests either bronchial leakage from the site of the removal of the cyst or the rupture of an additional bleb. It was thought inadvisable again to explore the thorax in this infant in view of the prompt and satisfactory response to suction alone.

SUMMARY

Symptoms produced by single large cysts of the lung are extremely variable but depend upon compression of residual nondiseased lung tissue, superimposed infection, hemorrhage, and spontaneous rupture of the cyst. The response to treatment depends upon the presence or absence of a lining of respiratory epithelium. In the presence of an epithelial lining obliteration of the cyst cannot be anticipated until the bronchiolar fistulas are closed and the lining of the cyst removed. It is not possible to determine the presence or absence of an epithelial lining clinically. It is recommended that single large cysts of the lung be treated by simple excision of the walls of the space, closure of bronchiolar fistulas, and obliteration of the pleural space by re-expansion of the lung with catheter drainage and suction. Cases to support these recommendations are cited.

ADDENDUM

Since this paper was submitted for publication, three additional cases of giant cyst of the lung have been operated upon using the method described. One patient developed a postoperative hemothorax which responded to aspiration. There were no complications in the other cases, and all three patients have satisfactory results.

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EXPERIMENTAL TUBERCULOSIS

II. Effects of Ligation of Pulmonary Arteries on Tuberculosis in Monkeys

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In a previous report[1] we have described the effects of anastomosis between systemic and pulmonary arteries in monkeys with induced tuberculosis. As a further phase in a *systematic investigation of experimental alteration of the* circulation in pulmonary tuberculosis, this report is concerned with the effects of ligation of pulmonary arteries on tuberculosis in monkeys.

METHODS

In these experiments 23 healthy *Macaca mulatta* monkeys were used. All were selected from carefully segregated stock animals which had consistently shown negative reactions to repeated tuberculin tests. Into each animal was injected through the saphenous vein a standard *suspension of the same virulent strain of Mycobacterium tuberculosis hominis* which was used in our previous experiments.

The infecting dose was given to one group of monkeys 18 to 24 hours before operation, and a comparable group of animals were infected 6 to 13 days after operation. In both groups of animals the operation consisted of (a) division of right or left pulmonary artery, or (b) division of branches of the pulmonary artery to the right or left upper lobe, and (c) control thoracotomy.

BACTERIOLOGIC TECHNIQUE

A virulent strain of *Myco. tuberculosis hominis* isolated by one of us (B. J. O.) at the National Institutes of Health was used in these experiments. The virulence of this strain, the details of culture, and the standardized technique employed in preparation of emulsions for animal inoculation have been discussed in a previous communication.[1] The dose of tubercle bacilli given intravenously to each monkey in the present experiments consisted of 1 c.c. of a suspension containing 10^{-4} milligrams of organisms. As may be seen in Table I the number of injected viable particles (single or clumped bacilli) ranged from 99 to 387. This degree of variation occurred despite every effort to insure uniformity in different preparations of emulsions during the 15 month period in which these animal inoculations were made.

OPERATIVE TECHNIQUE

Intravenous sodium pentobarbital anesthesia (30 mg. per kilogram) with morphine-atropine premedication was used. Pulmonary ventilation was maintained by means of a mechanical respirator which delivered oxygen through an endotracheal tube.[2] Aseptic surgical technique was used in all operations. After the hair had been clipped from the operative area, the skin was painted with tincture of iodine followed by alcohol. The chest was entered anteriorly through the fourth intercostal space on the left.

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In ligation of the pulmonary artery the vessel to the exposed lung was dissected free in the mediastinum and divided between ligatures.* In ligation of branches of the pulmonary artery to the upper lobe the artery to the exposed lung was dissected free in the mediastinum, and the superior branch of the artery was isolated, doubly ligated, and divided. Dissection was carried distally along the descending trunk of the pulmonary artery and any additional branches entering the upper lobe were divided. A small recurrent branch entering the inferior aspect of the hilum of the right upper lobe was regularly encountered in these monkeys.

In control thoracotomy the exposed lung was packed down with moist gauze for 15 to 60 minutes. In addition, in some of these animals the pulmonary artery was dissected free and occluded by a rubber shod clamp for a brief interval.

After each type of operation the lung was carefully re-expanded and closure of the chest wall was carried out in layers with interrupted silk sutures. Following operation each monkey was given intramuscularly 300,000 units of penicillin in oil. The animals were kept in separate cages in the same isolation room and were fed stock diet until their deaths.

RESULTS

There were no immediate postoperative deaths in the 23 animals submitted to operation. All wounds healed per primam and there was no instance of wound infection or empyema. Tuberculosis developed in each of the 23 monkeys and the disease was allowed to progress to a fatal termination.† A complete autopsy was performed immediately after death in each case. A special attempt was made to compare the character and extent of the tuberculous process in the lobe or lung on the side of arterial interruption with the lesions in the other pulmonary units of the same animal and with the lesions in the lungs of the control animals. Sections were taken from the lungs and other viscera for microscopic study. Color photographs were made as an aid in recording gross pathologic appearances.

Results Following Ligation of Right or Left Pulmonary Artery.—In 8 monkeys the right or left pulmonary artery was ligated. In 4 of these animals the infecting dose of tubercle bacilli was given 18 to 24 hours before operation. In the other 4 monkeys the bacilli were injected 6 to 13 days after operation. The monkeys lived from 66 to 376 days after inoculation. Pertinent data for these animals are summarized in Table I.

In 7 of the 8 animals with ligation of the pulmonary artery the extent of the pulmonary disease as seen at autopsy was greater in the lung on the side of the arterial ligation. Examples of the differences in the disease process in the two lungs are depicted in Figs. 1, 2, 3, and 4. In general, there were numerous conglomerate tuberculous lesions in the lung on the side of operation. This lung showed massive caseous areas in contrast to the opposite lung which presented smaller, less widely distributed tubercles, usually of the miliary type. In 6 of the 8 animals the lung on the side of operation was larger than the opposite lung. This increase in size is largely attributable to the greater amount of caseous tuberculosis in the lung. Figs. 1 and 3 are examples of this change in pulmonary volume due to massive tuberculous infiltration.

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*Throughout this report the term "ligation" will be used to indicate double ligation and division between the ligatures.

†One monkey died of an undetermined cause 18 days after ligation of the arteries to the right upper lobe. Autopsy showed only a few scattered miliary lesions in the liver.

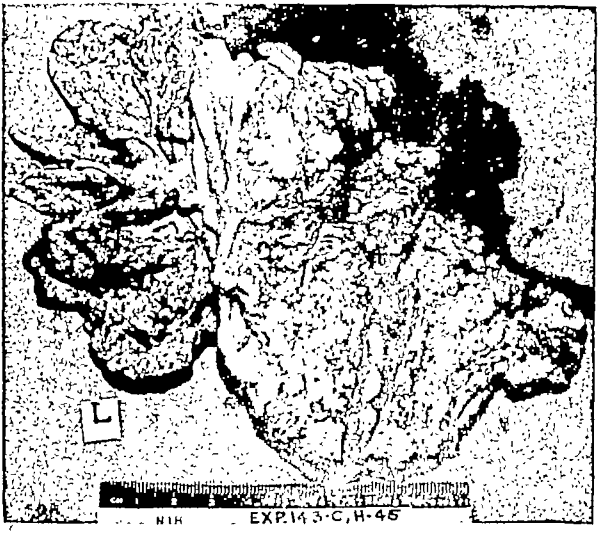

Fig. 1 (Monkey H-45).—Ligation of right pulmonary artery. Intravenous injection of tubercle bacilli on day preceding operation. Death 117 days later. Photograph of lungs at autopsy, showing confluent caseous tubercles in right lung; left lung shows only scattered miliary lesions.

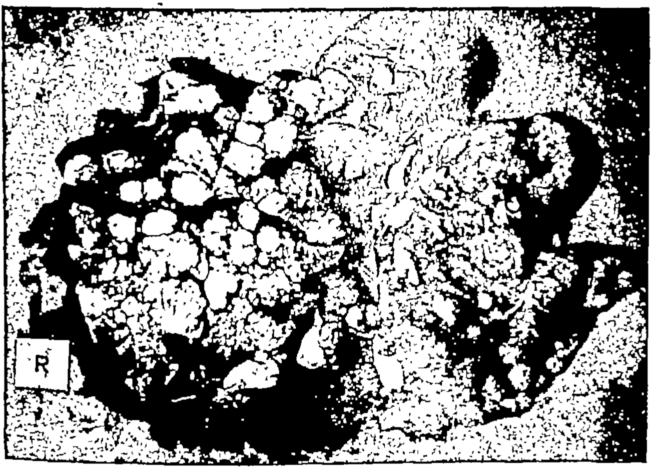

Fig. 2 (Monkey E-10).—Ligation of right pulmonary artery. Intravenous injection of tubercle bacilli on day preceding operation. Death 134 days later. Photograph of lungs at autopsy showing multiple large caseous foci in right lung. Tuberculous lesions are present in left lung but are smaller and less extensive than on the right. The projections from the cut surface of the left lung represent branches of the pulmonary artery filled with an injection mass introduced into the right ventricle at autopsy.

The extrapulmonary lesions in this group of monkeys were concentrated chiefly in liver, lymph nodes, and spleen, although scattered miliary lesions were distributed throughout many other viscera. Brain and meninges showed a few scattered miliary tubercles in 2 of these animals. Fig. 5 illustrates the lesions characteristically present in liver and spleen.

Microscopic study of sections from the lungs and other viscera of these monkeys confirmed the condition found at autopsy. Acid-fast stains demonstrated large numbers of tubercle bacilli in the lesions. There was a uniform lack of fibrosis around the areas. Microscopic examination of the lesions in the two lungs failed to show any significant differences which were not apparent from the gross examination.

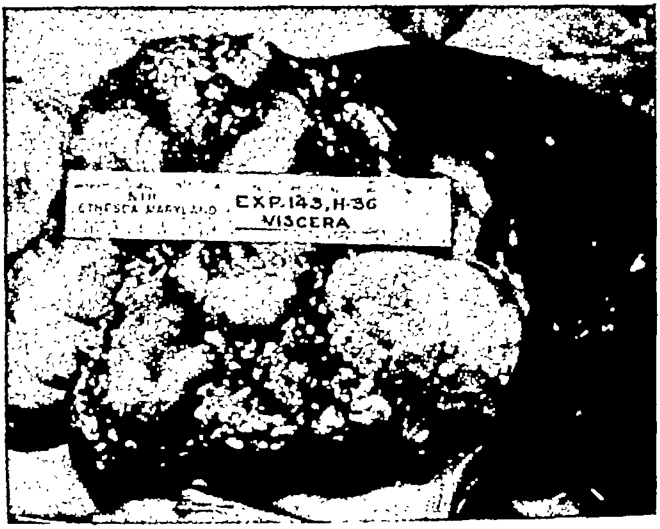

Fig. 5.—Photograph of abdominal viscera in a monkey with division of pulmonary artery to right upper lobe. Death 84 days after infection. The same general distribution is seen in all animals of these groups, although the liver is often more heavily involved.

Results Following Ligation of Branches of Pulmonary Artery to Right or Left Upper Lobe.—The branches of the pulmonary artery to the upper lobe of the right or left lung were ligated in 8 monkeys. In 4 of these animals the infecting dose of tubercle bacilli was given 18 to 24 hours before operation. In the other 4 monkeys the bacilli were injected 6 to 13 days after operation. One of these latter animals died 18 days after operation of an undetermined cause; autopsy showed only a few scattered 1 mm. tubercles in the liver. The other 7 monkeys lived from 72 to 177 days after injection, and in each animal extensive tuberculosis was found at autopsy. Pertinent data for these animals are summarized in Table I.

In 6 of the 8 animals with ligation of branches of the pulmonary artery to the upper lobe the extent of the pulmonary disease as seen at autopsy was greater in the upper lobe on the side of the ligation. Examples of the difference between the disease process in the affected upper lobe and that in the remainder of the lungs are shown in Figs. 6, 7, 8, and 9.

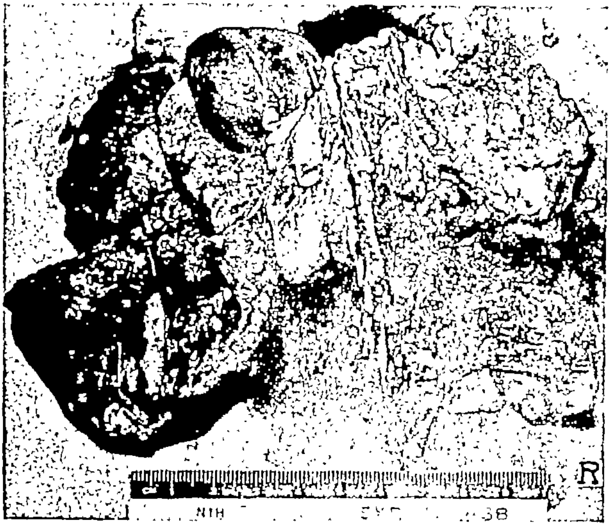

Fig. 6 (Monkey H-38).—Ligation of pulmonary arteries to upper lobe, right lung. Intravenous injection of tubercle bacilli 13 days after operation. Died 90 days later. Disease process more extensive in right upper lobe.

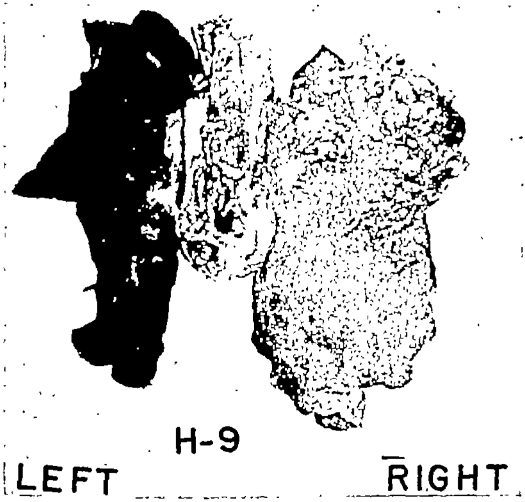

Fig. 7 (Monkey H-9).—Ligation of pulmonary arteries to upper lobe, right lung. Intravenous injection of tubercle bacilli 6 days after operation. Died 187 days later. Disease process more extensive in right upper lobe.

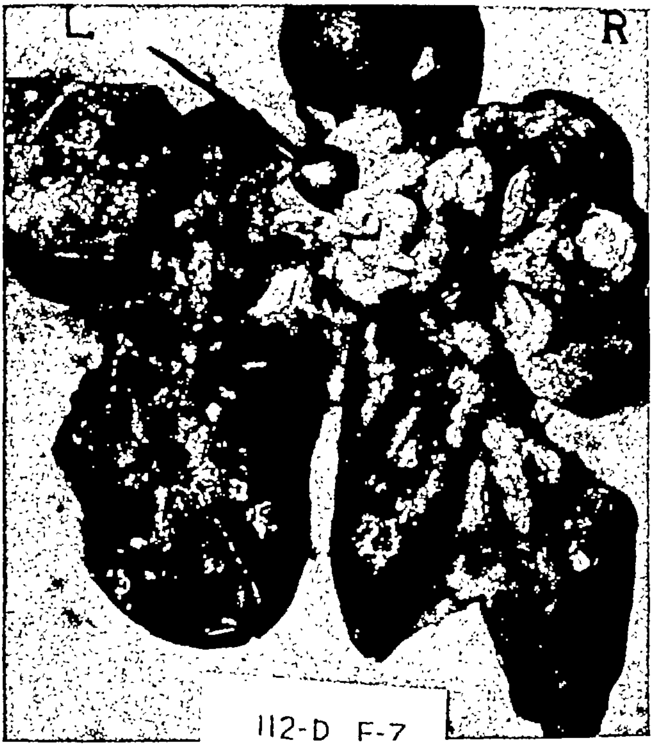

Fig. 8 (Monkey F-7).—Ligation of pulmonary arteries to upper lobe, right lung. Intravenous injection of tubercle bacilli 18 hours before operation. Died 177 days later. Large caseous foci in right upper lobe.

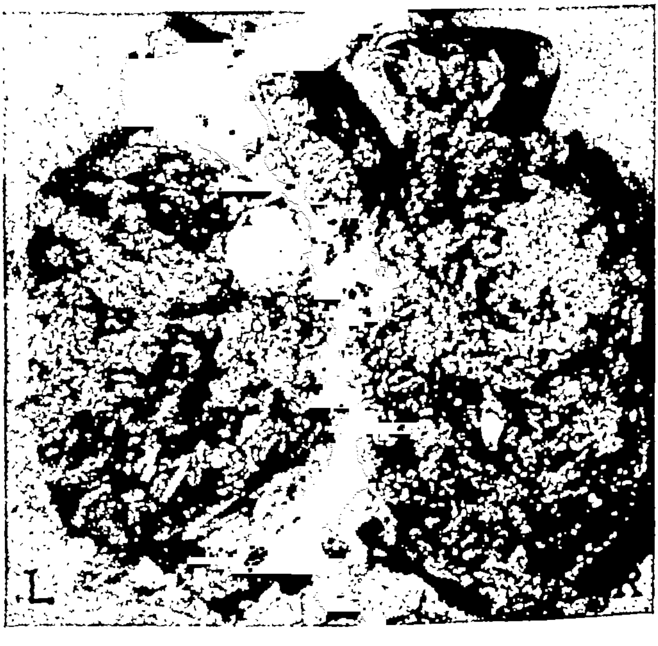

Fig. 9 (Monkey F-8).—Ligation of pulmonary arteries to upper lobe, left lung. Intravenous injection of tubercle bacilli 20 hours before operation. Died 162 days later. Large caseous focus in left upper lobe.

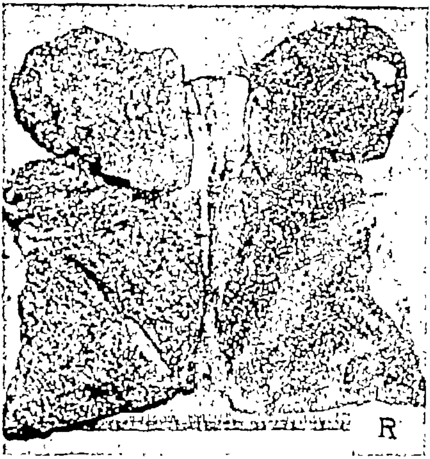

Fig. 10A (Monkey H-50).—Control thoracotomy, right. Intravenous injection of tubercle bacilli on day before operation. Died 119 days later. No essential difference between the lungs.

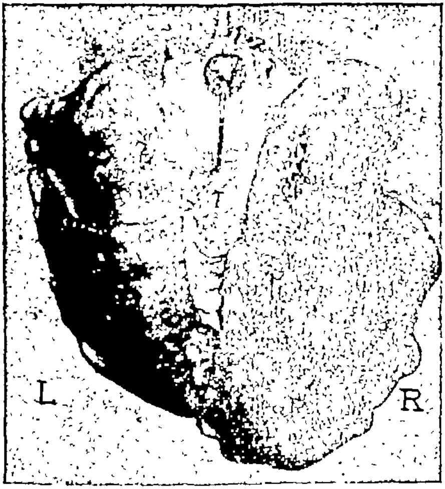

Fig. 10B (Monkey N-42).—Control thoracotomy, left. Intravenous injection of tubercle bacilli on day before operation. Died 98 days later. Lungs show equally distributed miliary lesions.

In general, the same changes in the disease process were found in the affected upper lobes of these animals as were encountered in the entire lung of the monkeys with ligation of the pulmonary artery. There were large conglomerate caseous masses in the upper lobe with arterial branches ligated in contrast to scattered small lesions in the remainder of the lung.

In 2 animals the disease process was of no greater extent in the upper lobe with ligated arteries. One of these monkeys received the infecting dose of organisms 13 days after the arteries to the upper lobe had been ligated. At autopsy there were seen symmetrically distributed small lesions throughout all lobes of both lungs. The second animal died so soon after inoculation (19 days) that there was no gross evidence of tuberculosis in the lungs at autopsy.

In these monkeys with ligation of arteries to the upper lobe the extrapulmonary lesions followed the pattern previously described in monkeys with ligation of the pulmonary artery. Microscopic study confirmed the observations made on gross examination. Tubercle bacilli were demonstrated in the lesions by acid-fast stains.

Results Following Control Thoracotomy.—In 7 monkeys thoracotomy was carried out but arterial ligation was not done. In all of these animals the lung was packed down for a brief period to simulate conditions existing during ligation of a pulmonary artery. Moreover, in 2 monkeys the pulmonary artery was dissected free and was occluded by a rubber shod clamp for a short time. Four of these monkeys were given the infecting dose of tubercle bacilli 18 to 24 hours before operation; the other 3 monkeys were infected 6 to 13 days after operation. These control animals lived from 76 to 150 days after inoculation. Results are summarized in Table I.

At autopsy the lungs of these 7 monkeys showed an equal distribution of tubercles of miliary type, ranging from 1 to 5 mm. in diameter. There were no observable differences between the two lungs from the standpoint of character or extent of the disease process, nor was there any difference in the extent or distribution of pulmonary tubercles in the monkeys inoculated before operation and in those inoculated after operation. Typical findings at autopsy in the lungs of these animals are illustrated in Fig. 10.

Extrapulmonary lesions in these control animals were similar in character and distribution to those in the monkeys with arterial ligations. Microscopic study of the lesions in the control animals demonstrated numerous tubercle bacilli and confirmed the condition observed at autopsy.

DISCUSSION

The results of this investigation indicate that in monkeys with induced tuberculosis, ligation of a pulmonary artery produces in the area supplied by the artery a pathologic process which differs from that in the remainder of the pulmonary tissue. When the artery to one lung is ligated, the disease process becomes more extensive in the lung on the side of ligation. When a lobar artery is ligated, the disease process in that lobe becomes more extensive than in the remaining lobes. Conglomerate caseous tuberculous lesions are found in the pulmonary unit thus deprived of a portion of its blood supply. In contrast, the remaining pulmonary tissue shows the miliary form of tuberculosis typically found in both lungs of control animals.

All of these animals were given the same dose (10^{-4} mg.) of the same strain of *Myco. tuberculosis hominis.* In all experiments the organisms were introduced through the saphenous vein. In half of the animals the infecting dose was given 18 to 24 hours before operation. This preoperative injection was designed to effect equal seeding of the two lungs with the initial dose of organisms.

In the remaining animals the organisms were injected 6 to 13 days after operation. It seems apparent that in those animals with ligation of the pulmonary artery to a lobe or to an entire lung, organisms injected after operation would be deposited in small numbers in the pulmonary unit thus deprived of its pulmonary arterial blood. Despite this smaller initial inoculum the disease process at autopsy was in most instances found to be more extensive in the lobe or lung with a ligated pulmonary artery. A summary of the over-all results of ligation of pulmonary arteries in both groups of monkeys is presented in Table II.

TABLE II. RESULTS OF LIGATION OF PULMONARY ARTERIES IN SIXTEEN MONKEYS WITH INDUCED TUBERCULOSIS

Lesions more extensive in lobe or lung with artery ligated	13
No difference in distribution of pulmonary lesions	2
Early death without gross pulmonary lesions	1

These effects of pulmonary artery ligation may be considered in relation to previous observations on this subject. In 1924, Schlaepfer[3] studied the changes in the uninfected lung of the dog after ligation of a pulmonary artery. On the basis of the fibrosis and shrinkage which occurred he concluded that ligation of a pulmonary artery might prove to be an effective means of treatment in human pulmonary tuberculosis. Hesse[4] has recently reported that partial occlusion of the main pulmonary arterial trunk resulted in increased susceptibility to tuberculosis in guinea pigs exposed to air-borne infection.

A few attempts have been made to modify the course of human pulmonary tuberculosis by ligation of a pulmonary artery. In 2 patients with cavitary tuberculosis Wilms[5] ligated the pulmonary artery with apparently beneficial results. Eloesser[6] in a report on surgical attempts at relief of severe hemoptysis in pulmonary tuberculosis, described a patient who was relieved of hemoptysis for 8 months after ligation of the pulmonary artery to the right upper lobe. Hemorrhage then recurred and the ultimate fate of the patient was not recorded. Rienhoff[7] in a recent publication mentioned a group of 8 patients with pulmonary tuberculosis in whom ligation of a pulmonary artery resulted in disastrous extension of the disease.

The results of the present experiments in monkeys with induced tuberculosis, together with the unfavorable results reported by Rienhoff, suggest strongly that ligation of a pulmonary artery is inadvisable in the surgical treatment of human pulmonary tuberculosis.

The changes produced in the disease process in this group of monkeys by ligation of pulmonary arteries are essentially the same as those which were encountered during an earlier phase of this investigation in the lungs of monkeys with diversion of systemic blood into a pulmonary artery. In the previous study[1] it was found that anastomosis between systemic and pulmonary arteries in monkeys with intravenously induced tuberculosis resulted in an extensive caseous form of the disease in the lung on the side of the anastomosis.

It is interesting that the same extensive caseous changes develop in the lung of monkeys with induced tuberculosis which undergo such widely different operative procedures as ligation of a pulmonary artery and anastomosis between a systemic and a pulmonary artery. These procedures appear to produce in the lung on the side of operation similar favorable conditions for progression of the disease.

A lung with a ligated pulmonary artery is supplied only by the bronchial artery. In contrast, a lung with a systemic-pulmonary anastomosis is supplied not only by the bronchial artery but by the arterial blood flowing through the anastomosis. There is obviously a greater blood flow to the lung under the latter condition. In both cases, however, the lung on the side of operation is perfused only by fully oxygenated blood in contrast to a normal lung which receives a mixture of oxygenated and unoxygenated blood. Thus, it is possible that the caseous pulmonary changes encountered in monkeys with pulmonary artery ligation and in those with systemic-pulmonary anastomosis are related to high oxygen tension in the blood perfusing the lung on the side of operation. Further work is required to evaluate the importance of this and other factors which may be related to these changes in the tuberculous process.

SUMMARY

In a series of 23 monkeys tuberculosis was induced by intravenous injection of human tubercle bacilli. The effect of ligation of the pulmonary arteries in these animals has been observed. In 7 of 8 monkeys with interruption of the pulmonary arterial blood supply to an entire lung there resulted an extensive, caseous tuberculous process in that lung, in contrast to the scattered miliary lesions found in the opposite lung.

Similarly, when the pulmonary artery to a single lobe was ligated, an extensive caseous process developed in that lobe in 6 of 8 animals. In contrast, scattered miliary lesions were found in all other lobes on both sides.

In 7 monkeys with induced tuberculosis which were submitted to simple thoracotomy, the tuberculous process was uniformly miliary in type with no difference between the lung on the side of operation and the opposite lung.

There is no essential difference between a group of monkeys given the infecting dose of organisms on the day preceding operation and a comparable

group infected 6 to 13 days after operation. The caseous tuberculous process which was observed after ligation of pulmonary arteries is similar to that which we have described after anastomosis between systemic and pulmonary arteries in monkeys. The possible relation of these changes to increased oxygenation of the blood perfusing the lung in these two instances of altered pulmonary circulation is noted.

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PULMONARY FUNCTION BEFORE AND AFTER EXTRAPLEURAL PNEUMOTHORAX

A Comparison With Other Forms of Collapse and Resection

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THE primary aim of any collapse procedure or resection in the treatment of pulmonary tuberculosis is arrest of the disease. Operative mortality and morbidity, complications or deformities, and late statistics further influence the fate of any particular method of treatment. In the choice of procedure preservation of pulmonary function as another factor has been increasingly recognized during the past twenty years. Collapse and resection procedures which are most selective and interfere least with ventilation are now known to carry a smaller operative mortality and are followed by a smoother convalescence. Furthermore, such "parenchymal-sparing" operations can be made available to a group of patients with very advanced or bilateral disease whose pulmonary reserve is such that only the most "selective" of procedures can be tolerated. Finally, such procedures cause less disability and therefore offer a greater opportunity for the patient to be restored to economic usefulness.

The effect on pulmonary function of many presently employed collapse procedures has been investigated. These reports to some extent have been responsible for the decline in popularity of such therapeutic measures as pneumothorax, and have prompted phthisiologists and thoracic surgeons to look for modifications of thoracoplasty in order to avoid paradoxical movement of the chest wall. Other forms of therapy, as pneumoperitoneum, have been received with great favor partly because of their complete reversibility and the small loss of pulmonary function incident to their administration.

The enthusiastic introduction of the modern extrapleural pneumonolysis followed by extrapleural pneumothorax by Schmidt[1] and Graf[2] was based to a great extent on the clinical observations of the "selectivity" of the procedure and the laboratory findings of Gaubatz[3] who showed that extrapleural pneumothorax caused relatively little loss of function.

Most investigators, since then, no matter what their opinion of the value of the operation as a whole, have agreed that extrapleural pneumothorax is selective and hence can be made available to patients whose pulmonary reserve is such that they could not tolerate thoracoplasty. They have further gen-

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erally observed that dyspnea after this operation is uncommon and a few who measured vital capacity before and after operation found the loss small. Similar observations concerning extrapleural plombage were made by Alexander sixteen years ago. He performed such an operation on a patient with a vital capacity of 800 c.c. without ill effect.[4] Like experiences have been reported recently when some of the newer plombage materials were used.[5]

The only recorded study of the effect of extrapleural pneumothorax on pulmonary function was made by Gaubatz in 1938.[3] Maximum breathing capacity, vital capacity, residual air, and oxygen debt were studied before and less than one month after operation in 77 patients. Improved function was reported after operation in 24 per cent of the patients, unchanged function in 33 per cent, and the remainder showed a loss of function of no more than 10 per cent. He compared these results with those after thoracoplasty and phrenic interruption and concluded that extrapleural pneumothorax and oleothorax caused less loss of function than either of the other operations.[6] No reports on the physiologic effect of extrapleural pneumothorax have appeared in this country.

We have undertaken to study the effects of extrapleural pneumothorax on pulmonary physiology for several reasons: (1) the advent of newer methods of study of residual air and of split function by bronchospirometry; (2) the availability for comparative purposes of a large number of other types of collapse procedures studied at the same postoperative intervals and by the same methods of investigation; (3) the possibility of comparing extrapleural pneumothorax not only with thoracoplasty but with medical collapse procedures and with newer types of treatment, particularly resection; (4) the paramount importance of comparing the effect of various collapse measures on lungs with comparable pathologic lesions; and (5) the recent renewed interest in extrapleural pneumothorax.[7, 8] This renewed interest has been stimulated by the availability of antibacterial agents,[9] the potential usefulness of the procedure as a preliminary to thoracoplasty,[10] and the increasing demand for more "selective" collapse procedures that will avoid the paradoxical movement of the decostalized chest wall and offer maximal preservation of function.

METHOD

Selection of Patients.—Extrapleural pneumothorax was carried out on 30 occasions on 28 patients with the following three indications (Table I): (1) previous contralateral collapse therapy with resulting contralateral limitation of function making the use of other collapse procedures inadvisable (12 cases). In general, we have hesitated to perform thoracoplasty or resection if the involved lung carried more than 60 per cent of the total function, no matter what the total function might be. (2) Bilateral cavitary disease of such nature that the necessity of eventual bilateral collapse therapy appeared great (13 cases). (3) As a preliminary to a modified type of thoracoplasty (5 cases) requiring extrapleural pneumothorax as a first stage, as used by Harken and Cincotti.[10]

Operative Procedure.—A standard extrapleural pneumonolysis through the bed of the fourth posterior rib was performed on all patients.[11, 12, 13] The dissection on the mediastinal aspect was carried down to and over the azygos vein on the right and the arch of the aorta

TABLE I. INDICATIONS FOR EXTRAPLEURAL PNEUMOTHORAX; VITAL CAPACITY AND RESIDUAL AIR BEFORE AND AFTER OPERATION

CASE NO.	AGE (YEAR)	SEX	CONTRALATERAL LUNG	VITAL CAPACITY (LITERS)				RESIDUAL AIR IN C.C.	
				NORMAL	PREOP.	14 DAYS POSTOP.	6 MONTHS POSTOP.	PREOP.	POSTOP.
				Group 1					
1	21	F	50% pneumothorax	3.25	1.92	1.56	1.60	—	—
2	31	F	70% hydropneumothorax	2.99	2.14	1.86	1.90	—	—
3	17	F	Pneumothorax, cavitary disease	3.37	1.81	1.58	—	—	—
4	36	F	Unexpandable pneumothorax lung	2.94	1.66	1.55	1.38	—	—
5	34	F	Pneumothorax, cavitary disease	2.91	2.01	2.00	2.00	—	—
6	34	F	Pneumothorax, cavitary disease	3.04	1.51	1.36	1.95	—	—
7	24	F	No lung	3.25	1.36	1.01	1.09	720	200
8	39	M	90% pyopneumothorax	3.88	2.78	2.22	2.48	1,100	480
9	44	M	10 rib thoracoplasty	4.25	1.88	1.56	—	1,650	920
10	23	M	Cavitary disease	4.36	3.20	2.55	2.85	1,240	820
11	23	M	Extrapleural pneumothorax	4.36	2.85	2.42	2.45	820	415
12	41	M	Effusion, atelectasis	3.97	2.90	2.10	2.39	—	—
13	35	M	Effusion, unexpanded lung	4.25	3.40	2.86	2.68	1,110	710
14	49	M	Cavitary disease	3.66	2.95	2.45	2.58	1,360	810
15	49	M	Extrapleural pneumothorax	3.66	2.58	2.01	—	810	625
16	39	M	Cavitary disease	4.09	3.13	2.45	2.43	—	—
17	33	F	Cavitary disease	3.00	3.17	2.34	2.60	—	—
18	40	M	Cavitary disease	3.95	3.73	3.16	3.20	1,400	910
19	50	M	10 rib thoracoplasty	3.92	1.70	1.52	—	—	—
20	37	M	Cavitary disease	4.23	2.70	2.35	—	—	—
21	22	F	Cavitary disease	3.32	2.32	1.99	—	—	—
22	61	M	"Normal"	3.85	3.05	2.95	3.06	—	—
23	40	F	"Normal"	2.88	3.03	2.58	2.5	1,620	1,105
24	37	F	"Normal"	2.80	2.15	1.84	1.90	970	715
25	46	M	"Normal"	3.90	3.65	3.12	3.26	1,100	820
26	20	F	"Normal"	3.39	2.98	2.43	2.80	1,005	510
27	26	M	Cavitary disease	4.16	1.68	1.58	—	—	—
Mean				3.59	2.77	2.25	2.42	1,145	695
				Group 2					
28	38	M	Surgical decortication	4.17	2.38	0.90	—	—	—
29	42	F	4 rib thoracoplasty	2.72	1.85	0.80	—	—	—
30	52	F	Cavitary disease	2.65	1.58	0.75	—	—	—
Mean				3.18	1.94	0.82	—	—	—

on the left. Postoperative care was identical to that by others except that all spaces were tapped dry assiduously and 500,000 units of penicillin and 0.5 Gm. of streptomycin were injected into the extrapleural space daily for two weeks.

Operative Results.—Four patients have had previously planned conversions to thoracoplasty. The space was lost in 4 patients for various reasons making postoperative management of the spaces unsatisfactory. The remaining 20 patients carry 22 extrapleural spaces. There have been no deaths, operative or otherwise, no bronchopleural fistulas, no extrapleural empyemas, and no spreads or reactivations.

Ventilatory Studies.—A detailed outline of ventilatory studies as performed in our laboratory has been reported elsewhere.[14] All patients were studied immediately prior to and fourteen days after operation and six months later after having been on walking exercises for two months. A few of the recently operated patients and those in whom thoracoplasty conversion was planned, were restudied as early as two months after operation.

Resting minute ventilation, vital capacity and its subdivisions, minute oxygen consumption, and the ventilatory equivalent were obtained from spirograms made with a closed circuit water spirometer with the patient breathing oxygen in the supine position. Vital capacities were also determined in the upright position. The maximum breathing capacity[15] was collected with a high velocity respiratory valve and a Douglas bag.[16] The walking ventilation was obtained in like manner during moderate exercise—walking on a level at the rate of 180 feet per minute for three minutes. The walking index was calculated according to the formula $\frac{\text{walking ventilation in liters/minute}}{\text{maximum breathing capacity in liters/minute}} \times 100$.[16] All tests were performed in triplicate and the best effort was recorded. Volumes were corrected to 37° C. Predicted normal values for vital capacity and maximum breathing capacity were calculated according to the regression formulas of Cournand and associates.[17] The air velocity index, previously described by one of us (E. A. G.), was calculated according to the formula $\frac{\text{per cent of predicted maximum breathing capacity}}{\text{per cent of predicted vital capacity}}$.[18] The normal value for this index is 1.0. Significantly smaller values indicate slowing of the expiratory air stream due to loss of elasticity of the lung or bronchial obstruction,[19] while larger values than 1.0 indicate greater than normal ventilatory efficiency. The latter are usually encountered with pathological or surgical loss of pulmonary parenchymal tissue. Residual air was determined with some modifications by the open circuit oxygen breathing method of Darling and associates.[20]

Bronchospirometry.—This was carried out immediately prior to operation in all but three patients. One of these had a previous contralateral pneumonectomy and the other two had severe recurrent hemoptyses continuing at the time of operation. The technique described by Jacobaeus[21] was carried out with a Zavod double lumen catheter[22] and oxygen was supplied with a Gelmuer twin spirometer.[23] Occasionally patients were allowed to breathe ambient air and the expired air was collected in Douglas bags and analyzed.[24] The same method was used in each patient before and after operation.

RESULTS

Results will be discussed in two sections. In the first, changes in pulmonary function will be reported after 27 operations during which the pleura was not opened, or, if opened, no intrapleural pneumothorax resulted either because of adhesions in that area or because of immediate postoperative intrapleural catheter drainage with underwater seal. The second group will deal with three cases in which the pleura was opened at operation with a resulting intrapleural hemopneumothorax which persisted for at least two weeks in spite of assiduous postoperative aspirations (Table I).

Group 1

Ventilatory Studies.—The mean maximum breathing capacity before operation was 84 liters per minute or 78 per cent of the mean predicted value. Fourteen days after operation it was 80 liters per minute and six months after operation 85 liters per minute. Thus postoperatively there was a drop of maximum breathing capacity of only 5 per cent and eventually there was no loss but a net gain. The great variability of functional results seen after thoracoplasty was here absent.[25] The largest single loss encountered at any time after operation was 17 per cent and that occurred in a patient who had had a previous contralateral pneumonectomy (Case 7, Table II).

The mean vital capacity before operation was 2.77 liters, or 77 per cent of the mean predicted figure. Preoperative ventilatory impairment, as meas-

TABLE II. MAXIMUM BREATHING CAPACITY, WALKING VENTILATION, AND WALKING INDEX BEFORE AND AFTER EXTRAPLEURAL PNEUMOTHORAX

CASE NO.	MAXIMUM BREATHING CAPACITY (L/MIN.)				WALKING VENTILATION (L/MIN.)	WALKING INDEX (PER CENT)		
	NORMAL	PREOP.	14 DAYS POSTOP.	6 MONTHS POSTOP.		PREOP.	14 DAYS POSTOP.	6 MONTHS POSTOP.
				Group 1				
1	96	71	72	74	20	28	28	27
2	84	85	87	88	18	21	21	20
3	106	57	60	—	22	39	37	—
4	85	72	71	73	17	24	24	23
5	86	65	65	68	13	20	19	19
6	90	58	53	73	17	34	—	23
7	100	65	54	56	21	32	39	32
8	109	83	63	78	17	20	27	22
9	143	52	48	—	21	40	44	—
10	123	115	96	119	16	14	17	13
11	123	119	108	107	16	15	15	15
12	116	61	57	67	18	30	—	27
13	122	102	94	91	13	13	16	17
14	98	90	90	91	14	16	16	16
15	98	91	86	—	14	16	18	—
16	134	131	121	126	16	12	13	12
17	101	90	88	101	16	18	18	16
18	112	121	108	116	17	14	18	17
19	109	39	37	—	16	41	43	—
20	142	66	62	—	28	42	45	—
21	91	64	61	—	18	28	29	—
22	121	121	119	121	23	19	19	19
23	98	85	78	88	19	22	24	21
24	82	77	86	84	14	18	13	14
25	123	102	103	113	24	23	23	21
26	102	105	104	125	15	14	14	12
27	123	51	53	—	12	24	23	—
Mean	108	84	80	85	18	24	25	23
				Group 2				
28	107	56	20	—	18	32	90	—
29	69	56	36	—	18	32	50	—
30	74	70	43	—	18	26	42	—
Mean	83	61	33	—	18	30	61	—

ured by vital capacity and maximum breathing capacity, was roughly the same. After operation the mean vital capacity dropped to 2.25 liters, a loss of 18 per cent, and six months after operation it was 2.42 (Table I).

The residual air, measured in 13 cases, showed a rather large decrease from a mean of 1.15 liters before operation to 0.69 liters after operation, a loss of 40 per cent. It is apparent that the extrapleural space is created chiefly at the expense of residual air (Table I).

The mean air velocity index (Table III) was slightly elevated to 1.12 before treatment, a not unexpected finding since many of the patients carried partially collapsed lungs preoperatively and all had advanced parenchymal disease.[18] Seven patients showed indices of less than 1.0. Bronchial asthma was ruled out in these by bronchodilator studies.[19] Pulmonary emphysema was confirmed by residual air determinations in three of the patients. Since there was no appreciable loss of maximum breathing capacity after operation, the air velocity index rose to 1.27 and showed a further small increase during the next few months. In other words, although the patients' lung volumes

TABLE III. BRONCHOSPIROMETRY AND AIR VELOCITY INDEX BEFORE AND AFTER EXTRAPLEURAL PNEUMOTHORAX

CASE NO.	BRONCHOSPIROMETRY, PER CENT FUNCTION OF OPERATED LUNG						AIR VELOCITY INDEX		
	OXYGEN UPTAKE		VENTILATION		VITAL CAPACITY				
	PREOP.	POSTOP.	PREOP.	POSTOP.	PREOP.	POSTOP.	PREOP.	14 DAYS POSTOP.	6 MONTHS POSTOP.
				Group 1					
1	77	71	75	62	72	62	1.25	1.56	1.57
2	72	65	58	59	74	67	1.42	1.66	1.64
3	34	34	38	39	36	36	1.00	1.21	—
4	65	55	64	59	73	58	1.52	1.65	1.83
5	45	43	55	53	56	54	1.10	1.15	1.15
6	—	—	—	—	—	—	1.28	1.31	1.27
7	100	100	100	100	100	100	1.55	1.74	1.65
8	85	82	70	73	89	84	1.07	1.02	1.12
9	86	86	65	58	72	69	0.82	0.92	—
10	77	53	74	55	72	52	1.29	1.34	1.49
11	47	36	45	35	48	39	1.49	1.57	1.58
12	40	33	58	35	52	31	0.73	0.92	0.97
13	53	46	61	46	65	44	1.05	1.15	1.19
14	52	50	49	40	54	41	1.14	1.37	1.31
15	50	51	60	51	59	51	1.31	1.60	—
16	50	45	22	18	30	26	1.29	1.50	1.58
17	40	35	51	44	46	35	0.84	1.11	1.15
18	34	34	37	18	36	23	1.14	1.20	1.29
19	96	91	68	65	80	79	0.84	0.87	—
20	—	—	—	—	—	—	0.76	0.77	—
21	36	32	34	30	29	24	1.00	1.12	—
22	35	29	44	43	45	41	1.27	1.29	1.27
23	38	37	45	40	39	39	0.83	0.89	1.00
24	36	36	57	51	38	42	1.22	1.59	1.50
25	38	37	56	47	46	37	0.88	1.05	1.09
26	40	34	62	38	46	36	1.17	1.42	1.48
27	—	—	—	—	—	—	1.05	1.27	—
Mean	56	51	56	48	57	49	1.12	1.27	1.29
				Group 2					
28	72	—	62	—	80	—	0.91	0.86	—
29	70	—	66	—	72	—	1.19	1.79	—
30	11	—	24	—	15	—	1.58	2.07	—
Mean	51	—	51	—	56	—	1.23	1.57	—

had decreased, they showed no loss of maximal ventilation and were therefore able to exchange more rapidly and more efficiently.[13]

The mean walking ventilation of 18 liters per minute corresponded fairly closely to the patients' metabolic requirements as expressed by surface area.[14] Only one patient (Case 20) showed an abnormally high ventilation during exercise. There was no significant change of walking ventilation after operation. The mean walking index, or percentage of maximum breathing capacity, which patients were required to use during this exercise was 24 per cent before operation. Several patients had indices of over 40 per cent and were therefore close to dyspnea at rest.[15] The mean walking index six months after operation was 23 per cent. In none of these patients, therefore, did extrapleural pneumothorax result in a disadvantage from the ventilatory standpoint.

Bronchospirometry.—Preoperative split function studies remarkably showed a larger share of the total function being carried by the lung to be operated upon. This was due to the fact that 12 of the 27 patients had had contralateral collapse therapy at the time of study, and most others had contralateral cavitary disease or effusion with unexpanded lungs. Only 4 of the group of 26 had "normal" contralateral lungs of the type one prefers to see prior to resection or thoracoplasty. The mean oxygen uptake, as per cent of the total, of the lungs to be collapsed was 56 per cent, the mean minute ventilation also was 56 per cent, and the mean vital capacity was 57 per cent of the total. These same values *after operation* were 51, 48, and 49 per cent, respectively. There was, therefore, a shift of function to the contralateral side of 5 per cent for oxygen uptake and of 8 per cent for ventilation and vital capacity. Even after operation, therefore, the operated lungs carried half of the total function.

Comparison With Other Collapse Procedures and Resection.—We have chosen to compare the preceding results with those obtained in our own laboratory after other operations rather than with those reported in the literature. This was done because we felt that although the testing procedures used by us are well standardized, nevertheless, variations in detail of technique from one laboratory to another are inevitable. Furthermore, all of our patients were studied at the same times—immediately preoperatively, 14 days and 6 months after operation. This made for more valid comparison. Last, many reports in the literature dealt with loss of function of individual patients and mean values but usually disregarded the type of lung on which the operation was performed. This, in our experience, is the single most important factor, as far as postoperative functional results are concerned—far more important than the number of ribs taken at thoracoplasty, or even the type of procedure itself.[25]

In Fig. 1 the functional losses 14 days after operation are compared regardless of the type of lung on which the operation was performed. The most severe impairment of ventilatory function was due to thoracoplasty in 121 instances with a loss of 26 per cent for maximum breathing and 35 per cent for vital capacity. This large loss immediately after completion of stages is partly due to collapse, and partly to paradoxical chest motion which is usually marked so soon after operation. Loss of function after 24 pneumonectomies and 20 lobectomies was almost as large as that after thoracoplasty. Phrenic interruption resulted in a 10 per cent decrease of maximum breathing capacity and an 18 per cent loss of vital capacity. Extrapleural pneumothorax, with a maximal space at this early postoperative period caused the least loss of ventilatory function—5 per cent for maximum breathing capacity and 18 per cent for vital capacity.

Of greater importance than the fourteen-day studies are the functional end results, as measured six months after operation (Fig. 2). Here the functional loss after pneumothorax was by far the greatest, larger than the loss with thoracoplasty 14 days postoperatively. Pneumothorax was not studied fourteen days after induction, since the desired shape and extent of collapse usually had not been obtained at that time. The functional end result of thoracoplasty was much better than the immediate result. Losses for both vital capacity and maximum breathing capacity were only one-half as large

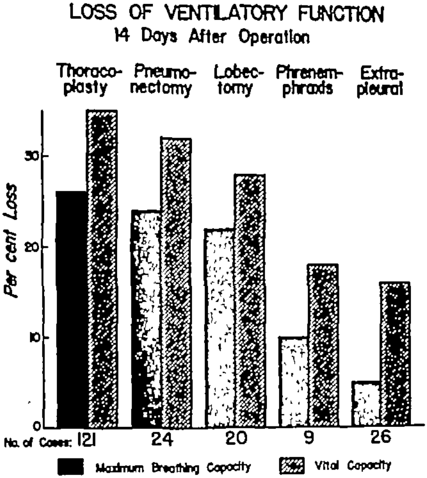

Fig. 1.—Per cent loss of maximum breathing capacity and vital capacity for various collapse procedures and resection 14 days after operation.

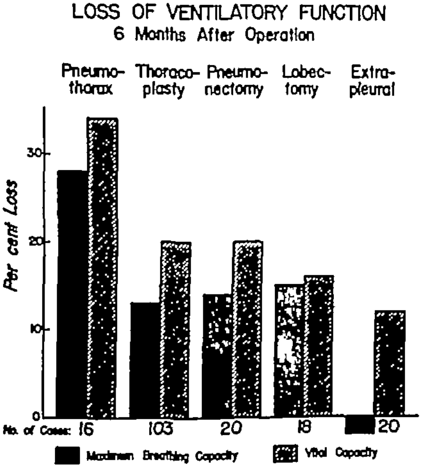

Fig. 2.—Per cent loss of maximum breathing capacity and vital capacity for various collapse procedures and resection 6 months after operation.

as immediately after operation. Patients with lobectomy or pneumonectomy showed considerable improvement during the further postoperative period, but this was not so marked as with thoracoplasty. Patients after phrenic interruption were studied six months after operation but motion of the diaphragm had usually returned by that time and results were therefore not included. Extrapleural pneumothorax patients, six months after operation, show a smaller decrease of vital capacity than after any of the other procedures and extrapleural pneumothorax was the only operation which caused no loss, but a small gain, of maximum breathing capacity.

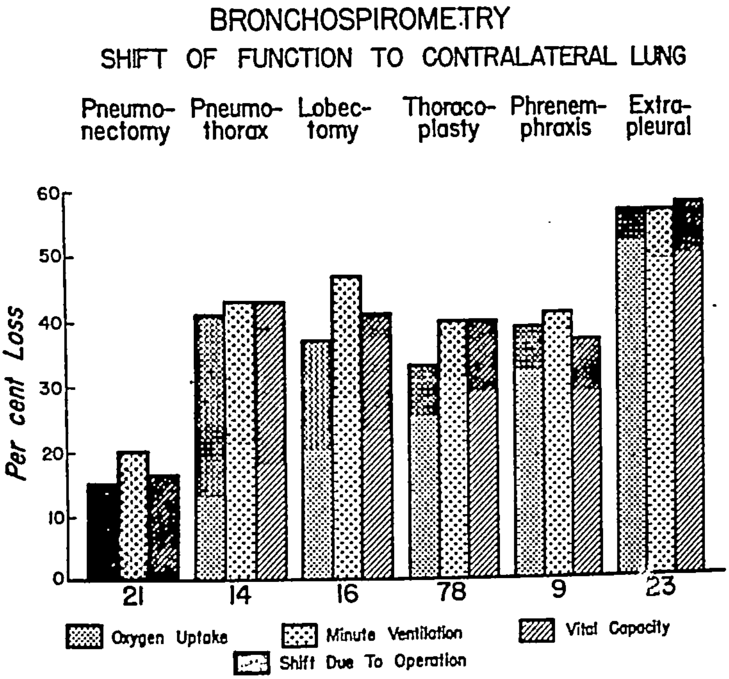

Fig. 3.—Shift of function to contralateral lung due to various collapse procedures and resection as determined by preoperative and postoperative bronchospirometry. The total height of the blocks represent share of total oxygen uptake, ventilation, and vital capacity of lungs before operation and the shaded areas represent shift of function to contralateral side due to operation.

The preceding studies are of interest in that they show what type of results were obtained with the various procedures as they were applied to individual cases. They are of no value for actual comparison since the type of lung for which the operations were performed were disregarded. The more nearly normal the function of the lungs, the larger the loss of function after collapse, no matter how collapse is obtained. This obvious fact has been shown by others and in our own laboratory.[25] Furthermore, the choice of procedure in many cases depended upon the share of function carried by the diseased lung. This is illustrated in Fig. 3. The total length of the blocks represents the share of the function-oxygen uptake, ventilation, and vital capacity—carried by the lung to be collapsed or resected. The shaded areas represent the shift of function to the other lung due to operation, as determined by bronchospirometry. It is apparent that most of our patients selected for pneumonectomy had almost useless lungs from a functional standpoint, and pneumonectomy was elected as the procedure of choice in many cases for that reason. The average share of the total oxygen uptake of pneumonectomy lungs was only 15 per cent. The function of lungs chosen for pneumothorax, lobectomy, and thoracoplasty varied from 30 to 40 per cent. At the other extreme were the extrapleural lungs with an average preoperative function of over 50 per cent. The shaded areas representing loss of relative function obviously cover the entire pneumonectomy area. Losses after pneumothorax, lobectomy, thoracoplasty, and phrenic interruption were strictly comparable since the operations were performed on the same type of lungs. These functional losses were greatest by far for pneumothorax and smallest for phrenic interruption.

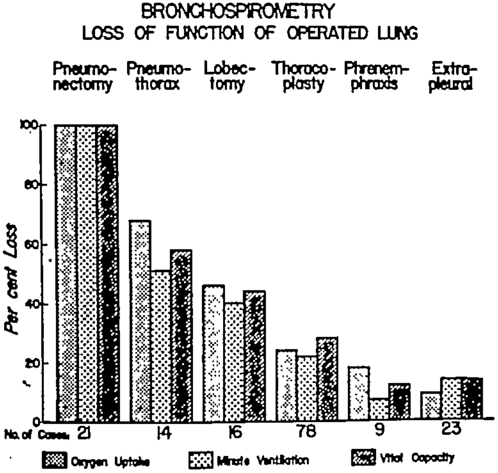

Fig. 4.—Function of lung to be operated upon was considered 100 per cent, no matter what the actual share of the function. The height of the blocks represent per cent loss of oxygen consumption, ventilation, and vital capacity after operation.

This last operation resulted in no appreciable loss of resting ventilation. This was also demonstrated by one of us (E. A. G.) with the aid of bronchospirometry during electrophrenic respiration.[26] The shift of function after extrapleural pneumothorax was relatively the smallest of all and the total shift compared favorably with that after phrenic interruption.

Comparison can be made in a different and perhaps more pertinent way from the same data: the function of the lung to be operated upon can be considered 100 per cent, no matter what the actual magnitude. From postoperative studies the per cent of loss of function of the involved lung can then be calculated. Fig. 4 presents data interpreted in this manner. After pneumonectomy, of course, the loss was 100 per cent. Losses in decreasing order were then found for pneumothorax, lobectomy, and thoracoplasty. Extrapleural pneumothorax caused the least loss of oxygen uptake while phrenic interruption caused the least loss of ventilation.

From bronchospirometric studies it was therefore possible to compare the loss of function after any particular procedure as applied to the same type of lung. Extrapleural pneumothorax was performed on lungs carrying over 40 per cent of the functional load in 18 of 27 patients. Fig. 5 presents a comparison of the losses of maximum breathing capacity and vital capacity of various operations on lungs which carried 40 per cent of the total oxygen uptake or more. There were few cases in our files of pneumonectomy done on such lungs. The only three illustrated were done for small malignant tumors. The same, to a lesser extent, applies to all other operations for 40 per cent lungs. Again in this group, pneumonectomy and pneumothorax led the decreasing order of functional losses. Thoracoplasty caused a poorer end result than lobectomy when compared in this fashion, a fact not apparent from the over-all charts of Figs. 2 and 4. The loss after phrenic interruption of such well-functioning lungs was also relatively great. Extrapleural pneumothorax caused the smallest decrease of vital capacity and resulted in a small gain of maximum breathing capacity.

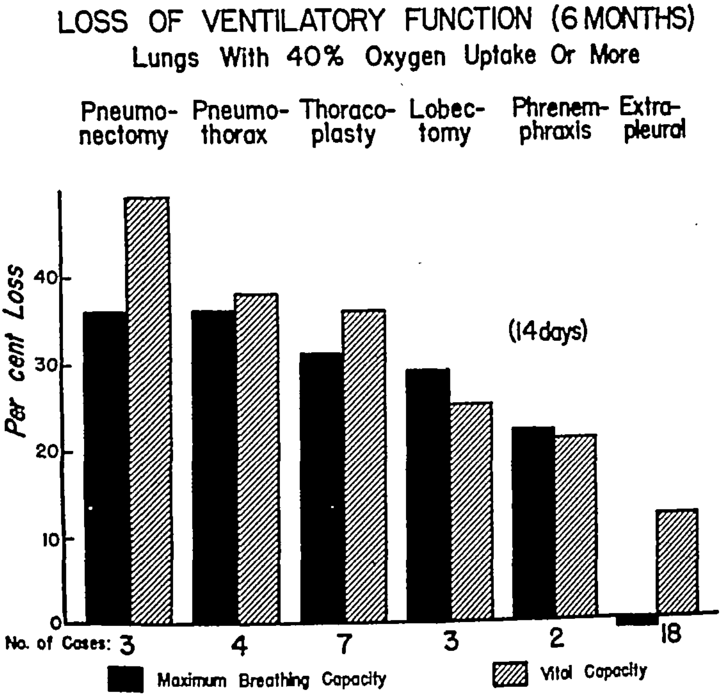

Fig. 5.—Per cent loss of maximum breathing capacity and vital capacity for various collapse procedures and resection performed on lungs which participated to the extent of 40 per cent or more in oxygen uptake before operation. Losses were calculated from six-month studies with the exception of phrenic interruption.

Individual Cases.—One of the difficulties in the physiologic evaluation of any particular type of surgical procedure is the estimation of the effect on the unoperated lung. A measured decrease in maximum breathing capacity or residual air, for example, may be due to the effect of collapse of the operated lung alone, it may be due to loss of function of both lungs, and it may be the end result of a combination of loss of function on the operated side and com-

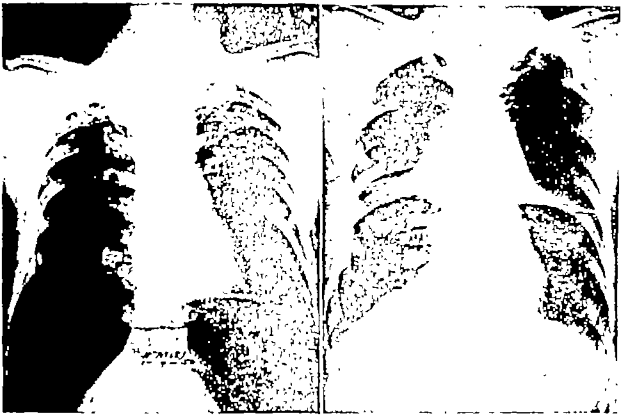

Fig. 6 (Patient No. 14-15).—Preoperative and postoperative posteroanterior roentgenograms of the chest.

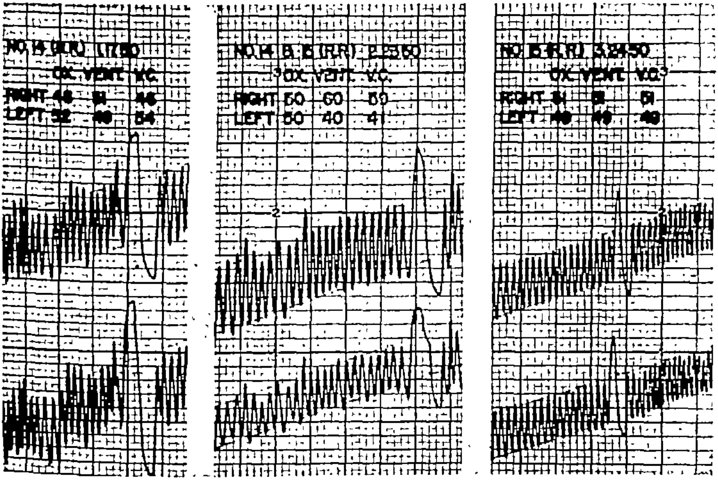

Fig. 7 (Patient No. 14-15).—Bronchospirometric tracings from left to right: before operation, after right extrapleural pneumothorax, and after bilateral extrapleural pneumothorax. Upper tracing: right lung.

pensatory gain on the other side. In the present series there were two patients on whom bilateral extrapleural pneumothorax was performed (Case 10-11 and Case 14-15); two patients where the contralateral lung was almost functionless (Cases 8 and 9); and last, one operation was performed on a remaining lung three years after contralateral pneumonectomy. No compensatory changes could occur here and the unique opportunity presented itself for study of the physiologic effect of the operation.

Fig. 6 shows the posteroanterior roentgenogram of the chest of patient No. 14-15 before and after bilateral extrapleural pneumothorax. Fig. 7 shows the bronchospirogram of the same patient before operation, after left extrapleural, and after both operations. The shift of function to the unoperated lung, unlike that after any other collapse procedure, here was hardly perceptible.

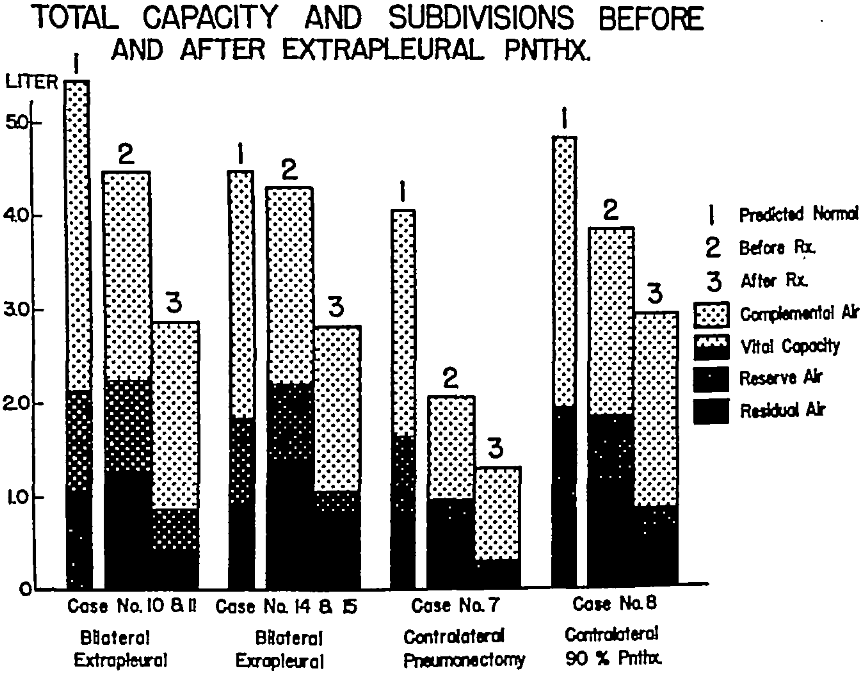

Fig. 8.—Predicted (*1*), preoperative (*2*) and postoperative (*3*) pulmonary total capacities and subdivisions. From left to right: Patients No. 10-11, No. 14-15, No. 7, and No. 8.

Fig. 8, section 2, shows the predicted total capacity and the determined values before and after both operations. The total capacity before operation was nearly normal but slight pulmonary emphysema was present. The ratio of 100 × RA/TC was 32, larger than the normal ratio of 24.[27] The decrease in the total capacity after operation was chiefly due to loss of functional residual air.

Total capacities before and after the other bilateral extrapleural pneumothorax in Case 10-11 are illustrated in Fig. 8, column 1. This patient's postoperative chest roentgenogram is included in Fig. 13. Physiologic changes of lung volumes were much the same as in the previous case. The initial total capacity was somewhat more reduced and again reduction after both operations was chiefly due to decrease of residual and reserve airs.

Patient No. 8 (Fig. 8, column 4) shows a surprisingly large total capacity in view of the fact that one of the patient's lungs was almost completely destroyed. Changes in the subdivisions of the total capacity were again much the same as in the previous cases, only here there was no reduction whatever of complementary air. The postoperative residual air volumes for the three cases of 625, 415, and 480 c.c., respectively, are, to our knowledge, the lowest values ever recorded.

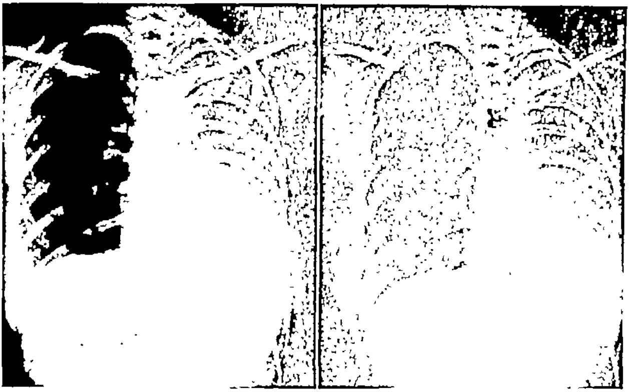

Fig. 9 (Patient No. 7).—Preoperative and postoperative posteroanterior roentgenograms of the chest.

The patient (Case 7) whose pre- and postoperative roentgenograms of the chest are recorded in Fig. 9 had had a left pneumonectomy three years prior to study with an operative spread to the contralateral apex. An oleothorax was induced on the left and the patient carried pneumoperitoneum for two years in an attempt to collapse a small right apical cavity and to control intermittent hemoptyses. A right extrapleural pneumonolysis with mediastinal dissection to the azygos vein was carried out eight months ago by one of us (J. W. S.) with sputum conversion. Gastric washings after suitable walking exercises have all been negative. This patient's maximum breathing capacity decreased from 65 to 56 liters per minute although from the appearance of the postoperative roentgenogram almost one-half the remaining lung appears collapsed. Since the exercise program was started, the patient has noted no dyspnea after rapid level walks and after climbing two flights of stairs. Her initial total capacity was one-half of normal (Fig. 8, column 3) with slight emphysema (100 × RA/TC:35). Again the complementary air remained almost unchanged and the residual air decreased from 720 to 200 [*sic*] c.c.

The last patient (Case 9) had a right ten-rib thoracoplasty several years ago (Fig. 10). Left apical cavitary disease was complicated by advanced pulmonary emphysema (100 × RA/TC:47) and he was slightly dyspneic even at rest. A small extrapleural pneumonolysis was performed in another institution.* Preoperative and postoperative bronchospirograms (Fig. 11) show no change in relative oxygen consumption. The patient's pulmonary mixing problem was improved since the 100 × RA/TC decreased from 47 to 37 and the complementary air was actually increased after operation because the residual air decreased more than the vital capacity.

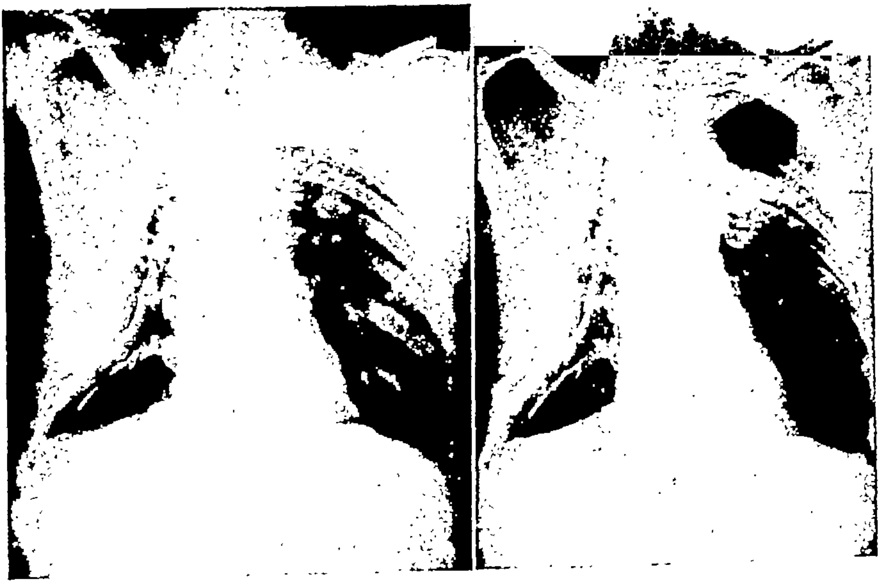

Fig. 10 (Patient No. 9).—Preoperative and postoperative posteroanterior roentgenograms of the chest.

Group 2

All three patients in this group had very limited respiratory reserve even before operation (Tables I and II). Two of the three showed over 70 per cent of the total function on the side under consideration for surgery (Table III). One of them (Case 27) had had a previous partially successful decortication of an unexpandable pneumothorax lung on the contralateral side and the other (Case 28) had an old four-rib thoracoplasty. In all three cases the pleura was accidentally opened at operation and intrapleural hemopneumothorax persisted for over fourteen days after operation in spite of assiduous and repeated aspirations. The postoperative functional picture here was entirely different from patients of Group 1. The mean vital capacity decreased from 1.94 to 0.82 liters fourteen days after operation, a loss of 58 per cent. The mean maximum breathing capacity decreased from 61 to 31 liters per minute, or 49 per cent. Two of the three patients (Cases 27 and 28) were severely dyspneic postoperatively and both remained on oxygen therapy for over two weeks.

A summary of the effect of parietal pleura tear at operation is given in Fig. 12. In 22 cases where this accident did not occur, the losses for vital capacity and maximum breathing capacity fourteen days after operation were 14 and 4 per cent, respectively. In 4 cases where the pleura was opened but intrapleural pneumothorax was avoided by intrapleural catheter drainage and underwater seal these losses were 23 and 14 per cent, respectively, while in the 3 cases just discussed the losses were 58 and 49 per cent.

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*Cambridge Sanatorium, Dr. Francis Woods.

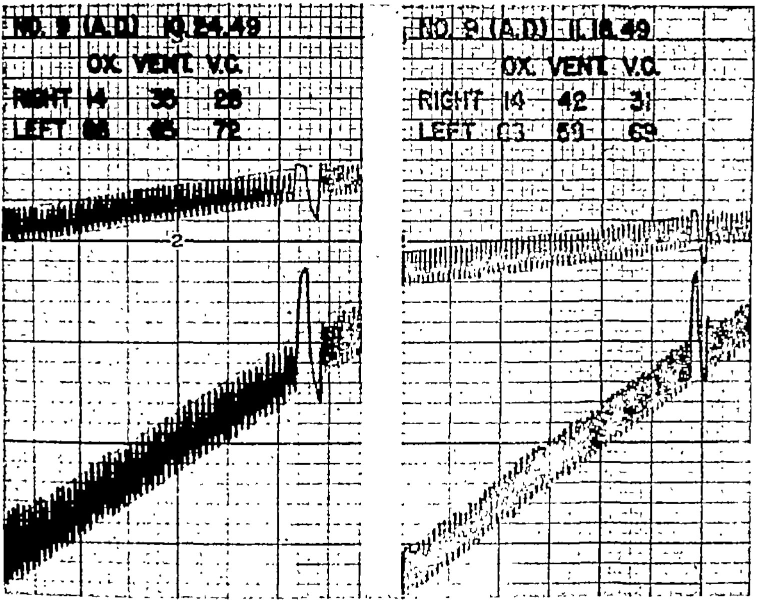

Fig. 11 (Patient No. 9).—Preoperative and postoperative bronchospirometric tracings. Upper tracing: right lung.

DISCUSSION

The aim of collapse therapy is to provide maximal collapse for diseased tissue with as little interference as possible with physiologic function of healthy lung tissue. Extrapleural pneumothorax conforms more closely to these aims than any other form of collapse therapy. There is minimal interference with ventilatory function as expressed by postoperative maximum breathing capacity. Collapse takes place almost exclusively at the expense of functional residual air.

It now remains to discuss the reasons for these striking functional end results. Following most forms of resection or collapse therapy losses of pulmonary function are encountered which are not due to collape per se but are due to a variety of undesirable physiologic alterations of the function of the chest wall, the diaphragm and mediastinum, and the pleura. Table IV presents an attempt at summarization of these effects for various types of collapse procedures.

TABLE IV. LOSS OF PULMONARY FUNCTION DUE TO FACTORS OTHER THAN COLLAPSE

	"MODERN" THORACOPLASTY	SUBCOSTAL PLOMBAGE	PULMONARY RESECTION	PHRENIC INTERRUPTION	INTRAPLEURAL PNEUMOTHORAX	PNEUMOPERITONEUM	EXTRAPLEURAL PNEUMOTHORAX
1. *Postoperative Period*							
Paradoxical motion of chest wall	++	+	0	0	0	0	0
Mediastinal swinging motion	++	+	0	+	+	0	0
Postoperative pain	++	++	+	0	0	±	±
2. *Persistent Changes*							
Interference with intrapleural pressure mechanism	0	0	0	0	++	0	0
Destruction of rib cage	++	++	0	0	0	0	0
Loss of diaphragmatic motion	+	+	+	++	0	+	0
Paradoxical motion of diaphragm	0	0	0	++	0	0	0
Compensatory increase of residual air (emphysema)	+	+	++	0	0	0	0
Residual pleural thickening and parietal fixation of lung	±	±	++	0	++	0	0

A number of factors are at play during the immediate postoperative period which are responsible for a greater pulmonary insufficiency as measured fourteen days after operation than six months after operation. These factors are chiefly pain due to interruption or traumatization of intercostal and other nerves, and paradoxical motion of the decostalized portion of the chest wall. Both of these factors are chiefly responsible for the great loss of function seen fourteen days after thoracoplasty (Fig. 1). Whether actual paradoxical motion of the air from one lung to the other (Pendelluft) also occurs with staged thoracoplasty is a matter of considerable debate. Subcostal, extraperiosteal plombage presents one of the many attempts of avoiding paradox seen after standard thoracoplasty.

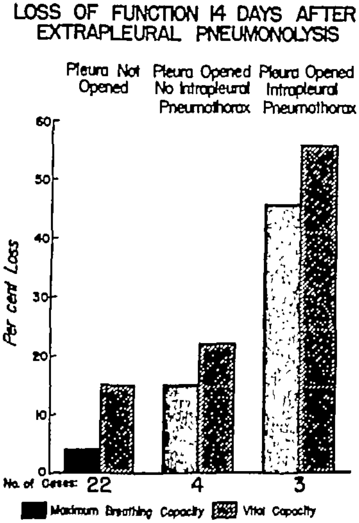

Fig. 12.—Per cent loss of maximum breathing capacity and vital capacity 14 days after extrapleural pneumothorax. From left to right: 22 patients in whom pleura was not opened during operation, 4 patients in whom pleura was opened but intrapleural pneumothorax was avoided, and 3 patients in whom pleura was opened resulting in marked hemopneumothorax.

In our experience this purpose is only partially accomplished. Pain after extrapleural pneumonolysis is usually minimal. Only a small segment of rib is removed, the intercostal nerve is left intact and the use of retractors and rib spreaders is avoided. Mediastinal swing after thoracoplasty is part of the paradox syndrome and is to some extent responsible for impaired function of both lungs. Its role after phrenic interruption has been previously discussed by one of us (E. A. G.). Suffice it to say here that the mediastinum can swing sufficiently under certain conditions to cause normal ventilation of a lung which is not otherwise caused to move either by the hemidiaphragm or the thoracic rib cage.[24]

There are a number of factors other than collapse responsible for persistent loss of function during the entire period the collapse is maintained (Table IV). The most important of these is interference with the intrapleural pressure mechanism. As long as the intrapleural space is merely a "potential" one, the surface of the lung must follow completely every motion of the diaphragm and rib cage. If only a small rim of intrapleural pneumothorax is created, a damping effect occurs which can be well visualized on fluoroscopy. The lung still follows the motion of the thoracic cage but only in a general way, its margin or surface moves less than the chest wall. An additional deleterious effect on the contralateral lung no doubt takes place due to mediastinal swing and altered intrathoracic pressure relationships. The end result of all these physiologic alterations on function can be seen not only from the various charts of comparative functional loss presented (Figs. 2 to 5), but are also evident from the changes which take place after uncomplicated extrapleural pneumothorax and after extrapleural pneumonolysis complicated by accidental intrapleural hemopneumothorax (Fig. 12).

Destruction of a portion of the thoracic cage, as encountered in thoracoplasty or extraperiosteal plombage, is deleterious to pulmonary function from three different aspects. The motion of the rib cage on the operated side is destroyed to a great extent even if the lower six or seven ribs are left intact, because the orderly sequence of the nervous mechanism of respiration is interrupted. The leaf of the diaphragm on the operated side becomes less efficient in its function since its full relaxation on expiration is ordinarily aided by a simultaneous contraction of the chest wall which exerts an infolding effect on the diaphragm.[26] A reduction in range of motion of the hemidiaphragm after thoracoplasty is always noted on postoperative fluoroscopy.[25] The third effect of a partially destroyed thoracic cage was recently pointed out by Cournand and associates.[20] The scoliosis due to thoracoplasty places the contralateral lung also at a relative mechanical disadvantage. Loss of diaphragmatic motion after pneumoperitoneum is never complete but occasionally quite marked. A decreased extent of motion is frequently found after lobectomy and after pneumothorax if the latter is complicated by hydrothorax. "Compensatory emphysema" of the remaining lobes after lobectomy and of the contralateral lung after pneumonectomy may play a role in the loss of function, particularly the respiratory component. This factor has been investigated for some years but a final answer to the problem is still to come.

From a comparison of the vertical columns of Table IV it is apparent that the physiologic disturbances enumerated previously involve extrapleural pneumothorax to a lesser extent than any other form of resection or collapse procedure used in the treatment of pulmonary tuberculosis. Fig. 13 shows postoperative roentgenograms of the chest of three of our patients in deep inspiratory and expiratory position. Preservation of diaphragmatic and rib cage motion is well illustrated. The extrapleural air space under positive pressure acts as a semisolid body which transmits the motion of the entire thoracic cage to the partially collapsed lung with the result that the maximal

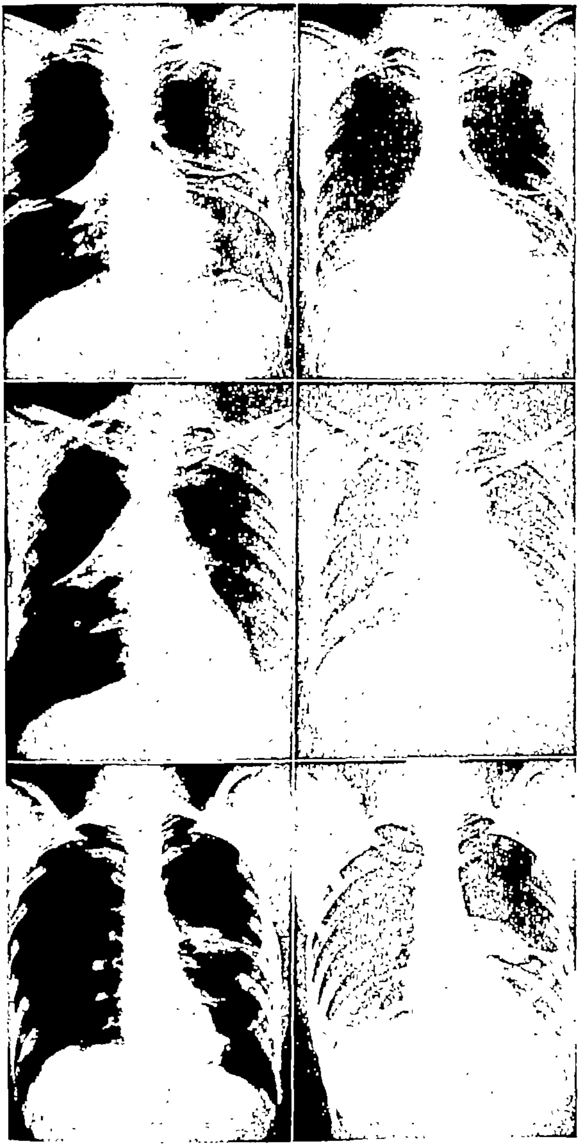

Fig. 13.—Posteroanterior roentgenograms of the chest on deep inspiration (left) and fullest expiration (right). Patients No. 10-11 (top of page), No. 13 (middle of page), and No. 26 (bottom of page).

air exchange remains unchanged and the extrapleural space is in effect subtracted from the residual air on expiration. The lungs in full expiration are almost devoid of air and in the roentgenogram have an almost atelectatic appearance. The floor of the extrapleural space can be seen to move several interspaces. This is best visualized on a kymogram.[6]

The authors are fully cognizant that the factors which place extrapleural pneumothorax in a favorable light functionally are the very factors which do not permit the desirable pulmonary "rest" in the sense of functional elimination.

Without entering the controversy concerning the indications for extrapleural pneumothorax, the data presented suggest that this operation can be carried out with the certain knowledge that the resulting loss of pulmonary function will be very small or nonexistent. The operation can, therefore, be offered to a number of patients whose pulmonary reserve would not permit any other type of collapse therapy. It is our hope that during the present re-evaluation of extrapleural pneumothorax both as a definitive procedure and as a preliminary to thoracoplasty these studies will aid in placing this operation in its proper light.

Although one cannot be other than enthusiastic solely on the basis of the comparatively favorable functional response to extrapleural pneumothorax, it is recognized that this procedure in itself is not a substitute at the present time for many of the proved collapse measures. Much time must elapse in order that opportunity shall be afforded the natural history of pulmonary tuberculosis to bring the end results into their proper perspective as it always has in any procedure which has been used to alter the course of any disease.

However, if the passage of time should show that single-stage extrapleural pneumothorax, freed of its complications by the use of biotherapeutic agents, offers at least as much to the patient as modern multiple stage thoracoplasty without comparable loss of function and deformity, the operation may well find its place as a leading contender in the choice of procedures.

SUMMARY

1. Loss of pulmonary function was studied by maximum breathing capacity, vital capacity, residual air, ventilation on exercise, breathing reserve, and bronchospirometry before operation and fourteen days and six months after operation of extrapleural pneumothorax on 30 occasions on 28 patients.

2. The loss fourteen days after operation was 18 per cent for vital capacity and 5 per cent for maximum breathing capacity, and the loss six months after operation was 12 per cent for vital capacity and there was a gain of 2 per cent for maximum breathing capacity. In 3 patients where the pleura was opened at operation with a resulting intrapleural hemopneumothorax the losses fourteen days after operation were 58 per cent for vital capacity and 49 per cent for maximum breathing capacity.

3. Bronchospirometric studies before operation showed an average function of 56 per cent of the total for the side to be operated upon since 83 per cent of the patients had contralateral collapse therapy or cavitary disease before operation. After operation there was a 5 per cent shift of oxygen uptake and an 8 per cent shift of ventilation and vital capacity to the contralateral lung.

4. Loss of function after extrapleural pneumothorax was compared to losses which occured after 121 thoracoplastics, 24 pneumonectomies, 20 lobectomies, 16 intrapleural pneumothoraces, and 9 phrenic interruptions. Both the total losses as calculated from maximum breathing capacity and vital capacity and the shift of function as calculated from bronchospirometry were smaller after extrapleural pneumothorax than for any other collapse procedure or resection studied. This was even more evident when operative losses were compared as performed on lungs with the same extent of preoperative function as determined by bronchospirometry.

5. Decrease of total pulmonary capacity after extrapleural pneumothorax took place chiefly at the expense of functional residual air.

6. Causes of loss of function other than that due to collapse for various operative procedures are discussed.

The authors take pleasure in acknowledging their indebtedness to Miss Dorothy M. Donnelly for her technical assistance.

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DISCUSSION

DR. VIKING OLOV BJÖRK, Stockholm, Sweden.—In the beginning of 1930, bronchospirometry was introduced by Jacobaeus, Frenckner, and Björkman. Since then the main difficulty has been to obtain large enough inner diameter of the tubes to prevent stenotic breathing and achieve reliable values. Pulmonary function studies at the Sabbatsberg Hospital in Stockholm have therefore been of practical value only since Carlens designed his double-lumen catheter.

(Slide.) You see the double-lumen catheter in place; it is provided with a small hook that is automatically engaged by the carina. This rubber hook is tied down to the catheter with a silk thread until it has been passed through the larynx, when the slipknot is untied. When the catheter is pushed down it automatically enters the left main bronchus. It is then easy to feel when the hook is engaged by the carina. Neither fluoroscopy nor bronchoscopy is necessary. Then the cuffs are inflated. The hook and the two rubber cuffs will maintain the catheter in the correct position. It cannot occlude the left upper lobe bronchus. The inner diameter is 7 mm. so that no stenosis is produced. Thus, the same value of the total capacity and its different fractions, both at rest and during exercise tests, are obtained when the values from the two lungs using the double-lumen catheter are added, as compared with the values obtained in the usual way with a mouthpiece. Also, the values of maximum breathing capacity are the same with the tube in place as without the tube.

It is as easy to introduce this catheter as an ordinary intratracheal tube for anesthesia, and it is now being used in the Crafoord Clinic as an ordinary anesthesia tube in cases with risk of spillover during operation.

(Slide.) This shows one lung anesthesia during lobectomy of a right upper lobe for an abscess. Continuous suction is applied.

(Slide.) When the bronchus is dissected and clamped, the rest of the right lung is connected with the spiropulsator and ventilated. This method is preferred to the face-down position.

DR. STRIEDER (closing).—I would simply like to say, in view of some comment in the corridors relative to extrapleural pneumothorax, that we do not propose it, as has been advocated in the past, as an operative panacea for tuberculosis. As Dr. Gaensler indicated, however, it is an operation which can be done when other operations cannot be done, and certainly in the experience of us all there are many such cases where the borderline residual function is such that a major procedure would certainly tip the patient over and make him a respiratory cripple, if he survived.

(Slide.) I would like briefly to show two such cases. The first is a 24-year-old white man who had pneumoperitoneum and bilateral cavitary disease for four years. The pneumoperitoneum was held until the second stage of bilateral extrapleural pneumothorax was completed.

(Slide.) This shows function studies before and after the right side, and after both sides, with a loss of some 7 liters of maximum breathing capacity. Vital capacity dropped from 3.2 to 2.4 liters, and breathing residual dropping only one per cent.

(Slide.) The second patient is a 24-year-old girl who had a total pneumonectomy on the left for a destroyed lung, some three years prior to her extrapleural pneumothorax. In the ensuing years she had developed the apical cavity which you see on the right and had intermittent hemoptysis with positive sputum. She also had a tuberculous empyema on the left which apparently had been controlled over the three-year period with oleothorax.

(Slide.) The maximum breathing capacity, before extrapleural pneumothorax, was 65 liters per minute, and it dropped only 9 liters, to 56, after extrapleural pneumothorax. The breathing reserve dropped from 68 cent to 62 per cent and, believe it or not, residual air was only 200 c.c. This girl is not dyspneic on mild physiologic exercise; she is walking comfortably on the level.

PULMONARY TUBERCULOMAS

Pathogenesis, Diagnosis, and Management

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THROUGH the increasing use of routine roentgen examinations of the chest, many solitary pulmonary masses have been discovered. These include both malignant and benign lesions. Tuberculomas represent the largest single group of these benign lesions. Tuberculosis of this type is rather loosely classified in the literature. There has been no complete statement clarifying the pathogenesis of this tuberculous process. Certainly no single explanation is adequate for all cases, and in any series the pathogenesis will vary from case to case.

Extrapulmonary tuberculomas have been adequately described. There have been, however, some inaccuracies in the use of the term, *pulmonary tuberculoma*. A tuberculoma is merely a tumorlike granuloma caused by the tubercle bacillus, encapsulated by connective tissue, and showing no evidence of surrounding inflammation or spread. These "tumors" may be completely or partially calcified, and may have many scattered caseating areas within the mass. They are usually oval or round in shape, and may vary from the size of a bean to the size of an orange, or larger. The term *tuberculoma* should probably be restricted to the tuberculous granuloma having a diameter of at least 2 cm. This is admittedly an arbitrary classification, but it serves to prevent further confusion in the literature as to the use of the term.

We believe that a pulmonary tuberculoma may arise in several ways:[12] (1) the encapsulation of a giant primary focus—this focus may occur at any age; (2) the encapsulation of a restricted reinfection focus of tuberculosis that has a tendency toward rapid regression, and that becomes homogeneous; (3) the completely blocked tuberculous cavity with resultant inspissation of caseous material, fibrosis, calcification, and shrinkage of the occluded cavity; this cavity may occur in the reinfection focus, and rarely in the Ghon focus.

Many theories have been advanced describing the mechanism responsible for the closure of tuberculous cavities, and undoubtedly cavities heal by different mechanisms. Coryllos has drawn attention to the closure of tuberculous cavities by means of bronchial occlusion. Auerbach and Green presented four cases in which closure and healing of tuberculous cavities occurred by bronchial occlusion. Loesch, in 1944, presented a detailed pathologic description of complete closure of cavities, and his pathologic findings are in close accord with those of Coryllos. The occlusion of a stem bronchus to a cavity may result in the formation of a tuberculoma. The bronchi which are tributary to the draining

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cavities are almost always involved by the tuberculous process to varying degrees of severity. This tuberculous process in the bronchi produces mechanical changes, chiefly narrowing or complete occlusion of the lumen. With a patent unnarrowed bronchus, there is a free passage of air to and from the cavity on respiration. As is well known, tension cavities often form with incomplete bronchostenosis. With complete occlusion of the bronchus there is gradual absorption of air within the cavity, and atelectasis in the area of lung supplied by the bronchus. The anoxemia of the atelactatic lung which suppresses ventilation and circulation will cause fibrosis. Eventually the wall of the cavity will be completely replaced by a fibrous tissue. The cavity may now fill in with caseous material, and be visible on the roentgenogram as a solitary circumscribed shadow. The fate of the erstwhile cavity is now uncertain. Pinner stated: "Cavities that become blocked by bronchial occlusion may sometimes, after long periods of blockage, reopen and produce bacilliferous sputum and intrabronchial dissemination." He presented roentgenograms of a case illustrating the reopening of a tuberculous cavity. On the other hand, regressive changes may occur, the caseous material becoming inspissated and perhaps calcified. Actual bone formation has been described in tuberculomas. Case 1 illustrates the method by which a bronchial communicating cavity becomes a solid tumor, most likely by means of a bronchial occlusion.

This paper is primarily concerned with tuberculomas within the pulmonary parenchyma; however, tuberculomas may occur within the mediastinum. The formation of a mediastinal tuberculoma is due to a caseating process in the mediastinal lymph nodes. Six cases of mediastinal tuberculoma have been reported in the literature.[13, 14, 25] Case 10, in the opinion of the operating surgeon, was a mediastinal tuberculoma, although pathologic evidence is lacking. Case 12 fits all the criteria for a diagnosis of mediastinal tuberculoma.

Tuberculomas have been described as occurring in the central nervous system, brain, orbit, middle ear, breast, stomach, nasal septum, paranasal sinuses, and abdominal wall and lungs. Tuberculomas of the pulmonary fields are not infrequent. In 1931, Albert described round foci which he believed represented encapsulated tuberculous lesions. In 1932, Straub observed eight cases of single and multiple round tuberculous foci. He observed that some of these would undergo changes only after a long period of time. Klein and Wolff, in 1934, added six more cases to the literature, five of which showed inactivity of the round foci after one or two years. One case which came to autopsy revealed a lesion which had remained stationary for about six months, only to break down and be the cause of a spreading exudative tuberculosis. At autopsy the characteristic lesion consisted of a chalky caseous substance encircled by more centrally deposited loose connective tissue and a peripheral dense hyaline connective tissue capsule. Birkelo and Kasper, in 1939, described the radiographic appearance and progress of the circular lesions of tuberculosis. Many of these lesions were stable and could be classified as tuberculomas. Maurer-Mast and Franklin, in 1941, reported a case of tuberculoma, and stated that there were only two cases of similar nature reported in the literature. However, many of the solitary round foci of tuberculosis described in the literature previous to this report were undoubtedly tuberculomas. Jones and Dolley, and Dieffenbach, in 1940, each reported a case of tuberculoma for which a total pneumonectomy had been done because of a mistaken diagnosis of bronchiogenic carcinoma. Since that time many tuberculomas have been described, notably in the surgical literature.[9, 10, 11, 26] Surgery, in many of these cases, was undertaken with a mistaken diagnosis of lung tumor. Mahon and his associates had in their series 35 patients treated by pulmonary resection, either lobectomy or wedge-shaped excision for tuberculoma.

The roentgenographic diagnosis of solitary shadows within the lung fields is frequently extremely difficult. While the roentgenographic visualization of the chest is invaluable for demonstrating the presence of a lesion, it cannot always be relied upon for an adequate differentiation. It is beyond the intent and scope of this paper to describe the complete roentgenologic findings of various tumors found within the lung fields.

The differential diagnosis of circumscribed solitary shadows within the lung fields must always include both primary and secondary neoplasms, tuberculomas, encapsulated effusions, cysts, abscesses, localized areas of pneumonitis, hamartoma of the lung, arteriovenous aneurysms, and other more rare lesions. Occasionally a neoplasm in the mediastinum will be drawn out into the lung fields by negative intrathoracic pressure. These tumors are usually benign, because malignant mediastinal tumors are fixed and remain within the mediastinum. Many of these lesions are uncommon, and others can be excluded by special x-ray techniques.

The solitary circumscribed shadow of the tuberculoma is readily confused with the peripheral type of pulmonary carcinoma. The two lesions, however, may occasionally be readily differentiated. The presence of calcification, to our knowledge, has never been observed roentgenographically within primary malignant tumors. The type of calcification seen radiographically in tuberculomas is variable. A tuberculoma may be so completely calcified that it resembles a giant mulberry. The calcification may be arranged as a single concentric ring at the periphery of the tumor, or in the form of multiple concentric rings. There may be discrete scattered areas of calcification throughout the tumor. Calcification which is not seen in ordinary projections of the chest may be visualized by tomographic studies. Other radiographic features which suggest the diagnosis of tuberculoma are multiple areas of diminished density throughout the tuberculoma which represent areas of caseation and adjacent areas of calcification and fibrosis. The tuberculoma is oval, round, or lobulated, and regular in outline. Rarely there may be multiple tuberculomas. Tuberculomas are often seen which are homogeneous in density, and do not contain any calcium. It will occasionally be noticed that this type of tuberculoma may enlarge when observed over a short period of time. It is the calcium-free tuberculomas which cannot be differentiated roentgenographically from bronchiogenic carcinoma of the peripheral type.

A bronchiogenic carcinoma may have a smooth, round contour and lie in the peripheral lung fields. It may have a homogeneous density, or it may have areas of diminished density from breakdown throughout the tumor. This type of bronchiogenic tumor apparently tends to grow by expansion rather than infiltration. However, it has been our experience that primary peripheral neoplasms in most instances show definite roentgen evidences of infiltration beyond the main mass of density. Completely encapsulated, noninfiltrative primary neoplasms are extremely rare as compared with tuberculomas and other benign lesions.

Tumors of the prostate, testicle, and kidney tend to metastasize to the lungs, and occasionally appear as solitary circumscribed lesions within the lung fields. Usually, however, within a few weeks multiple nodules appear in the lung fields and simplify the diagnosis. Thornton, Adams, and Bloch state that, although they see thirty multiple metastatic tumors per year, they have seen only three solitary metastases in ten years. There is no way of differentiating the slowly-growing metastatic lesion from a bronchiogenic carcinoma, except to search for a primary lesion. Rarely, multiple tuberculomas may occur in the lung fields and be mistaken for metastases to the lung. Dahl-Iverson and Møller reported a case in which two tuberculomas were present within the pulmonary parenchyma in the lower right lobe, one posterior and one anterior. We have seen one case in which two tuberculomas were present, for which lobectomy was done. Fortunately, these lesions were calcified, and a diagnosis of tuberculoma was made preoperatively. We have also seen another case in which a radiographic diagnosis of double tuberculoma was made. However, this case did not come to operation.

The greatest percentage of solitary peripheral masses, both with and without surrounding infiltration, will prove to be carcinoma of the peripheral type, which type constitutes approximately 25 per cent of all primary lung tumors. Thornton, Adams, and Bloch presented twenty-three cases of solitary "circumscribed tumors" which had been observed at the University of Chicago clinics in a ten-year period. Seventeen of these were malignant lung tumors, fourteen primary, three were metastatic. Six were benign, one hemangioma, four tuberculomas, one a chronic lung abscess. Since the majority of the solitary peripheral tumors are due to malignant disease, we must consider every lesion of this type malignant until proved otherwise, or we shall continue to fall into the errors of the past. Patients with bronchiogenic carcinoma are occasionally admitted to tuberculosis sanatoriums and the malignant process is far advanced before the correct diagnosis is made. Pillsbury and Wassersug reported on ten patients who were admitted to a tuberculosis sanatorium in a ten-year period, who were later proved to have had bronchiogenic carcinoma.

It is our belief that a more extensive and complete roentgenologic study would result in an almost absolute roentgen diagnosis of malignant neoplasm in many instances, for which immediate definitive therapy could be carried out.

The problem of deciding the best treatment for a patient who has been referred to a surgeon, with an asymptomatic, solitary, well-circumscribed mass in the lung field, is not always an easy one, and every weapon in our diagnostic armamentarium must be utilized. The patient should be fluoroscoped and roentgenograms taken. Tomography may be of value in demonstrating areas of calcification. Efforts should be made by the medical consultant to rule out primary neoplastic disease of other organs, particularly kidney, prostate, or testicle.

Bronchoscopy may have been completed without gaining further information or help, particularly when the tumor is inaccessible to the bronchoscope, as in a tumor located in a peripheral bronchus. Secretions obtained bronchoscopically and stained by the Papanicolaou technique may result in a high percentage of positive diagnoses. Herbut and Clerf reported thirty cases of primary pulmonary carcinoma in which the bronchial secretions were stained by the Papanicolaou technique. Cancer cells were demonstrated in twenty-two cases, or 73 per cent. Studies done on these bronchial secretions may result in the demonstration of tubercle bacilli. A tuberculin test should always be done. If enlarged peripheral nodes are detected, they should be biopsied. Intrapleural fluid, if present, should be aspirated and cytologic studies carried out.

Tuberculomas in the pulmonary fields may be classified roentgenographically into two general groups. This grouping is important because it will be of great value in determining the activity of the lesion, and will indicate the necessity and the urgency of surgery.

The first group is *tuberculomas without calcification.* These tumors may be homogeneous in density, or may show one or more central areas of diminished density. Sputum studies may be negative or positive for tubercle bacilli. Some of these cases, through mismanagement, may have been followed for periods of six months or more without roentgenographic change in the size or character of the lesion. These tuberculomas constitute a threat to the continued well-being of the patient, because of the danger of imminent spread of the tuberculous process to the surrounding lung tissues. Case 2 illustrates the spread of a tuberculous process which could have been prevented by the early surgical extirpation of the tuberculoma. It must be noted in cases with a peripheral lesion of this type that the possibility of a bronchiogenic carcinoma has not been definitely ruled out, although there has been no roentgenographic progression of the lesion. It is for these reasons that immediate surgery should be recommended for the solitary round tumor without calcification, with or without areas of central breakdown.

The second group is *tuberculomas with calcification.* This group may be further divided into subgroups, depending on whether or not they contain central areas of breakdown. The calcified tuberculomas with radiographic areas of central radiolucency may be the focus of a spreading tuberculous process, and surgery may be recommended for these cases. Asymptomatic patients who demonstrate well-calcified tuberculomas in the lung fields, without central areas of radiolucency and with negative sputa, are in little or no danger of having a spread of this tuberculous process, so surgery is not recommended; instead, the patient is followed for long periods of time by serial roentgenograms. In fact, surgical intervention may be the cause of tuberculous complications. Case 7 illustrates some of the complications which may occur following the removal of a calcified tuberculoma.

CASE REPORTS

CASE 1.—M. A. was a 74-year-old woman who had numerous hospital admissions for bronchial asthma during the past fifteen years. She had low-grade temperature and a productive cough, occasionally with blood-streaked sputum, during these asthmatic episodes. She had massive hemoptysis in 1943, and again in April, 1948.

In April, 1942, radiographic examination of the dorsal spine showed a sharply demarcated cystic area in the right upper lobe, posteriorly. This cystic area measured 7 by 5 by 6 cm. In August, 1943, roentgenographic examination of the chest at the bedside showed a triangular area of density extending outward from the upper right hilar area, with gradually diminishing density at the periphery of the chest. This change was believed to be due to infection surrounding and obliterating the cystic lesion. One week later there was some surrounding pneumonitis, and the cystic nature of the lesion was again recognizable. Re-examination at the bedside in October, 1943, showed no appreciable change in the lesion. The next examination was in June, 1947, and there was now a rounded density in the area where the cyst was previously noted. There was no appreciable surrounding inflammatory reaction in the pulmonary tissue. In April, 1948, the cystic area was almost completely filled by dense material. The only aerated portion of the cystic area which remained was superiorly and posteriorly. The lesion was sharply demarcated and showed no surrounding infiltration, with no demonstrable calcification. The last roentgenographic examination of the chest, in May, 1949, showed no appreciable change in this lesion since examination of 1948.

Smears, cultures, and guinea pig inoculations were constantly negative for tubercle bacilli. Bronchoscopic examination was not done.

Discussion.—This case illustrates one of the methods of tuberculoma formation, and shows the transformation of a tension air-filled cavity to an almost solid tumor. This was probably due to the progression from partial to complete bronchial occlusion.

CASE 2.—G. H., a 32-year-old man, was examined roentgenographically by a mobile chest unit in April, 1946. A large circular area of increased density was noted at the level of the first interspace and second rib anteriorly on the right. There was no calcification in the mass. The remainder of the lung fields appeared clear. The patient had no symptoms or physical findings at that time. The diagnosis was undetermined, and interval studies directed.

The patient returned to the chest clinic in July, 1947, for a repeat roentgenogram, which showed no change since first examination. The impression at that time was that this lesion was most likely a tuberculoma. In April, 1948, he complained of weakness and fatigue. A roentgenogram of the chest was made, which showed a diffuse exudative lesion involving the greater portion of the right upper lobe. This had the appearance of a moderately advanced pulmonary tuberculosis with cavitation. Re-examination on June 23, 1948, showed further increase in the infiltrative lesions in the right upper lobe.

Sputum studies showed tubercle bacilli on smear and culture. The patient was sent to a tuberculosis sanatorium.

Discussion.—This case demonstrates the lurking malevolence of pulmonary tuberculomas. The possibility of either a malignant tumor or a tuberculoma should have been considered. In a tuberculoma without calcification the danger of spread into contiguous lung tissue cannot be over-emphasized. A thoracotomy should have been done in 1946 when this mass was first discovered.

CASE 3.—A. S., a 22-year-old white man, in February, 1946, was discovered to have a "spot on his lung." He was hospitalized for about four and one-half months at another institution, without any change in the size of the shadow. On discharge he had some shortness of breath and pain over the lower ribs on the right anteriorly. In January, 1947, he developed a productive cough, and had blood-streaked sputum on two occasions. Physical examination was essentially negative.

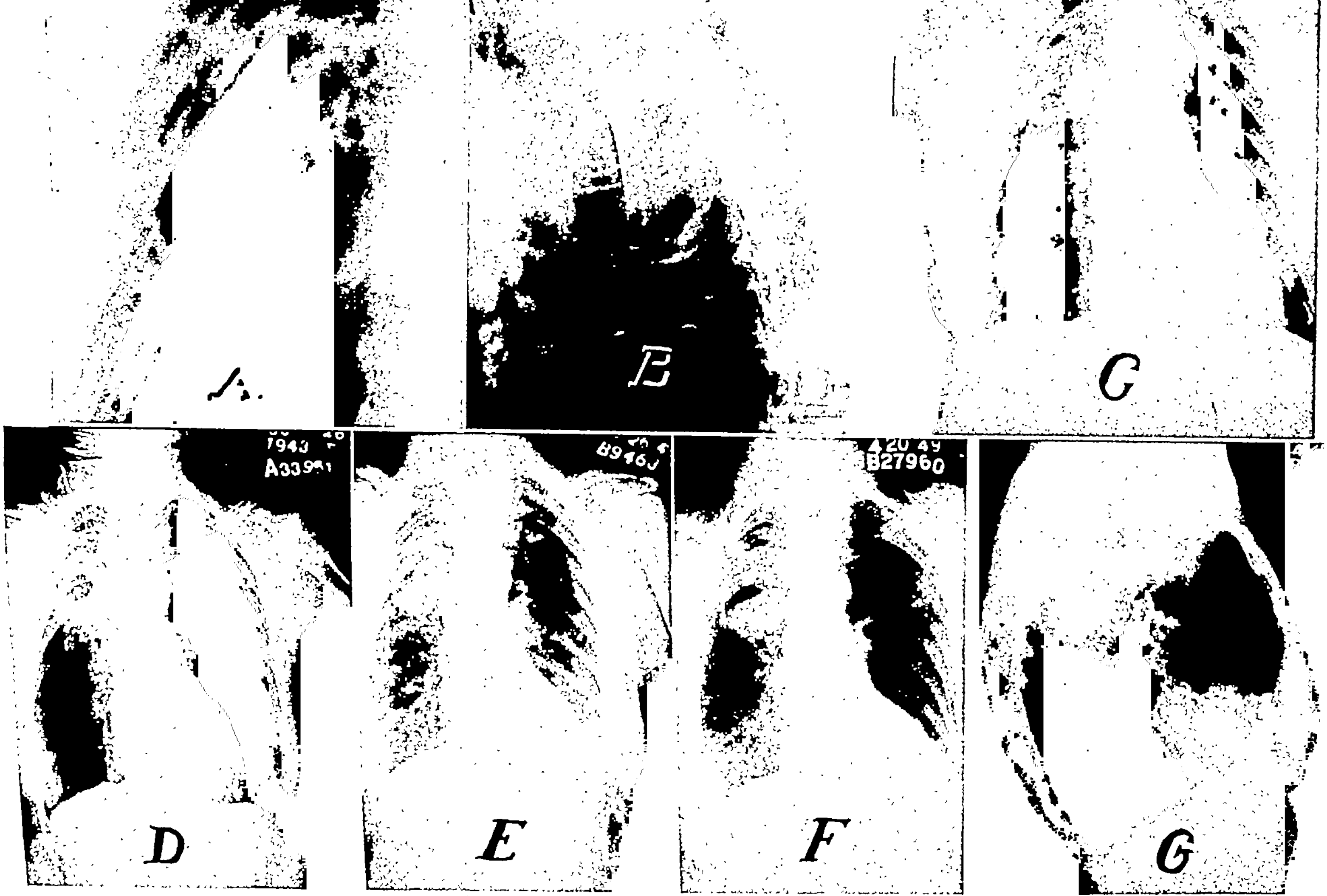

Fig. 1 (Case 1).—Demonstrates the evolution of the air-filled cystic lesion in the right upper lobe into an almost solid tumor mass.
A, and *B*, Roentgenograms taken in April, 1942. A large cystic lesion is present in the right upper lobe.
C, Roentgenograms in August, 1943. There is some surrounding pneumonitis about the cyst.
D, Roentgenogram in October, 1943.
E, Roentgenogram in April, 1948.
F and *G*, Posteroanterior and lateral roentgenograms in April, 1949, show the previously cystic lesion to be almost completely filled in by dense material. No calcification could be demonstrated within this mass.

Roentgenographic examination of the chest showed a well-circumscribed lesion in the apical portion of the right lower lobe. This measured two inches in diameter and had an area of breakdown in the center. No calcification was seen in the mass or in the lung fields.

Direct smears and cultures were positive for tubercle bacilli. Bronchoscopic observation showed the right middle lobe bronchus orifice to be a slit about one-half the usual size. The bronchus was stenosed below this middle lobe orifice.

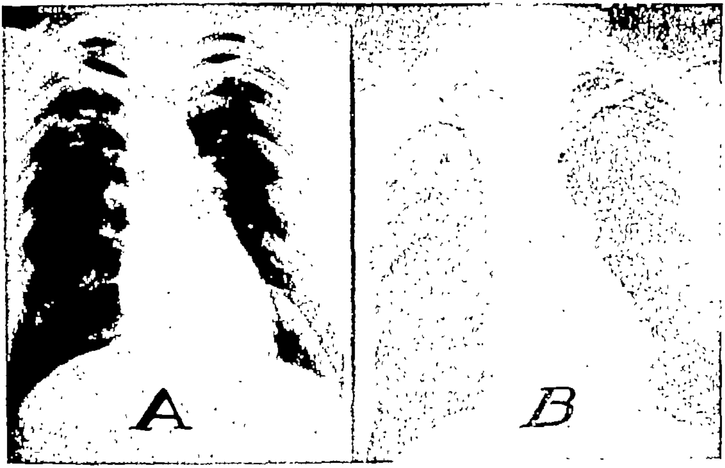

Fig. 2 (Case 2).—*A*, Roentgenogram in July, 1947 showed a circumscribed mass in the right upper lobe. No calcification or areas of breakdown could be demonstrated in this mass.

B, Roentgenogram on April 1, 1948, demonstrated a diffuse exudating lesion involving the greater portion of the right upper lobe.

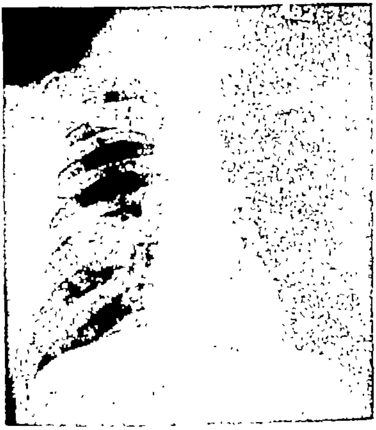

Fig. 3 (Case 3).—Roentgenogram of chest showing right lower lobe mass with breakdown.

On the fourteenth hospital day a right thoracotomy was done. In the lower and middle lobes there was a hard, nodular tumor which did not have the consistency of a malignant tumor. The lower and middle lobes were resected.

This proved pathologically to be a tuberculoma with cavitation and active tuberculous granulation tissue in the surrounding atelectatic lung. Smears from the central cavity showed a large number of tubercle bacilli.

Discussion.—This case demonstrates a tuberculoma with central cavitation. This tuberculoma was in imminent danger of spread. Despite the positive sputum studies and because of the lack of calcification within the tumor mass, the possibility of a bronchiogenic carcinoma with central breakdown was never excluded. In either case, immediate surgery was the treatment of choice.

CASE 4.—N. S., a 57-year-old white man, was referred by his physician to a clinic in another city because of complaints of parasthesias in both legs. A chest film taken there in 1946 was read as essentially negative. This roentgenogram was reviewed at that clinic in January, 1948, and a question was brought up as to whether there was a tumor mass in the chest, or whether this was merely a soft tissue shadow.

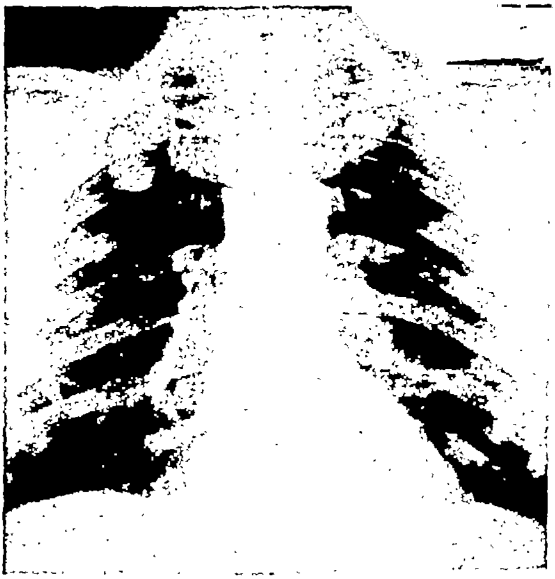

Fig. 4 (Case 4).—Roentgenogram demonstrates an oval mass in right upper lobe. No calcification or breakdown seen.

Because of this questionable finding, a radiographic examination of the chest was done in 1948 which revealed an oval mass 3½ by 3 cm., in the right upper lobe posteriorly. The mass was homogeneous in density. There was no calcification, nor were there any areas of radiolucency in this mass. The previous roentgenograms of the chest which were taken in 1946 were reviewed. The mass in the chest was present at that time, and there had been no change in the size of the mass in the ensuing sixteen months.

Bronchoscopic observation was negative. Cultures and guinea pig inoculations of bronchial aspirated secretions were positive for tubercle bacilli.

It was recommended that this patient have an exploratory thoracotomy; however, he refused surgery.

Discussion.—This lesion is most likely a tuberculoma, and of the type which is liable to undergo spread at any time, although it may remain dormant for years. In view of the tubercle bacilli in the sputum and the lack of calcification in the tumor mass, definitive surgery should have been done. However, the patient refused to have any surgical procedures carried out on his chest. It must also be noted that the time interval alone does not rule out a primary neoplastic process. This patient was seen in February, 1950. He was asymptomatic and the chest film was unchanged.

CASE 5.—A. D., a 52-year-old white man, was seen in January, 1949, with a history of a weight loss of twenty-five pounds in the last two years, and a nonproductive cough for six months. Physical examination was essentially negative.

Roentgenographic examination of the chest revealed a solitary rounded mass in the left upper lobe. The outermost border of the lesion was rather indistinct, and seemed to infiltrate the pulmonary fields. There was an area of undiminished density in this tumor mass. There were calcific areas in the hilar nodes.

Bronchoscopic observation was negative. Guinea pig inoculations and cultures from bronchoscopically obtained secretions were positive for tubercle bacilli.

An exploratory thoracotomy was done in March, 1949. There was a tumor mass lying in the upper lobe, apparently arising from the upper lobe main-stem bronchus. It was slightly rubbery in consistency, and there were no outlying regions of metastasis. After study of the pathologic report, the operating surgeon was not sufficiently convinced that the lesion was of neoplastic origin, and he felt that a lobectomy would be a more conservative procedure. If a malignant tumor was found on dissecting the lobe, the surgeon then intended to proceed with the pneumonectomy. On sectioning the lobe, the mass was found to be a typical tuberculoma, and therefore the lower lobe was inflated and the chest wall closed.

The tumor proved pathologically to be a typical diffuse caseated tuberculoma with distinct fibrous encapsulation and with a corona of epithelioid giant-cell tubercles at the periphery. In central portions there was extensive necrobiosis

Discussion.—The preoperative diagnosis was a pulmonary tuberculoma. In view of the positive culture for tubercle bacilli, and the area of radiolucency in the center of the tumor mass, immediate surgery was the treatment of choice. This patient was seen in March, 1950. He was asymtomatic. No pulmonary complications had developed.

CASE 6.—O. G., a 49-year-old white woman, was hospitalized in September, 1948, because of a mass found in the chest during a routine survey by a mobile chest unit. In 1944, this patient had been treated with intracavitary radium and external radiation for a grade 3 carcinoma of the cervix, with complete regression and no recurrence of the lesion. The patient had no symptoms referable to the chest, and physical examination was essentially negative.

Roentgen examination of the chest showed a small lesion, 2 cm. in its greatest diameter, in the right lower lobe. There was a calcium deposit around the periphery of the lesion. There was a small calcific deposit in the sixth interspace posteriorly on the left. There were multiple areas of calcification in the hilar glands. This lesion conformed to a roentgenographic impression of tuberculoma.

No bacteriologic studies were done.

It was felt by the surgical department that this mass could be a solitary metastasis or a tuberculoma. In view of the patient's excellent health, and because the lesion was in the periphery of the lung, it was decided to admit her for exploration and removal of the mass. An exploratory thoracotomy was done in March, 1949. On entering the chest, a puckered area was seen in the right lower lobe. Since this could not be indentified grossly, it was decided to remove the indurated area. This was sharply dissected out with digital pressure on the surrounding lung parenchyma.

The removed tumor was 2 cm. in diameter, grayish in coloration, and fairly soft in consistency. It was a firmly encapsulated, fibrocaseous, and extremely chalky tuberculoma. No active tuberculous granulation tissue was seen.

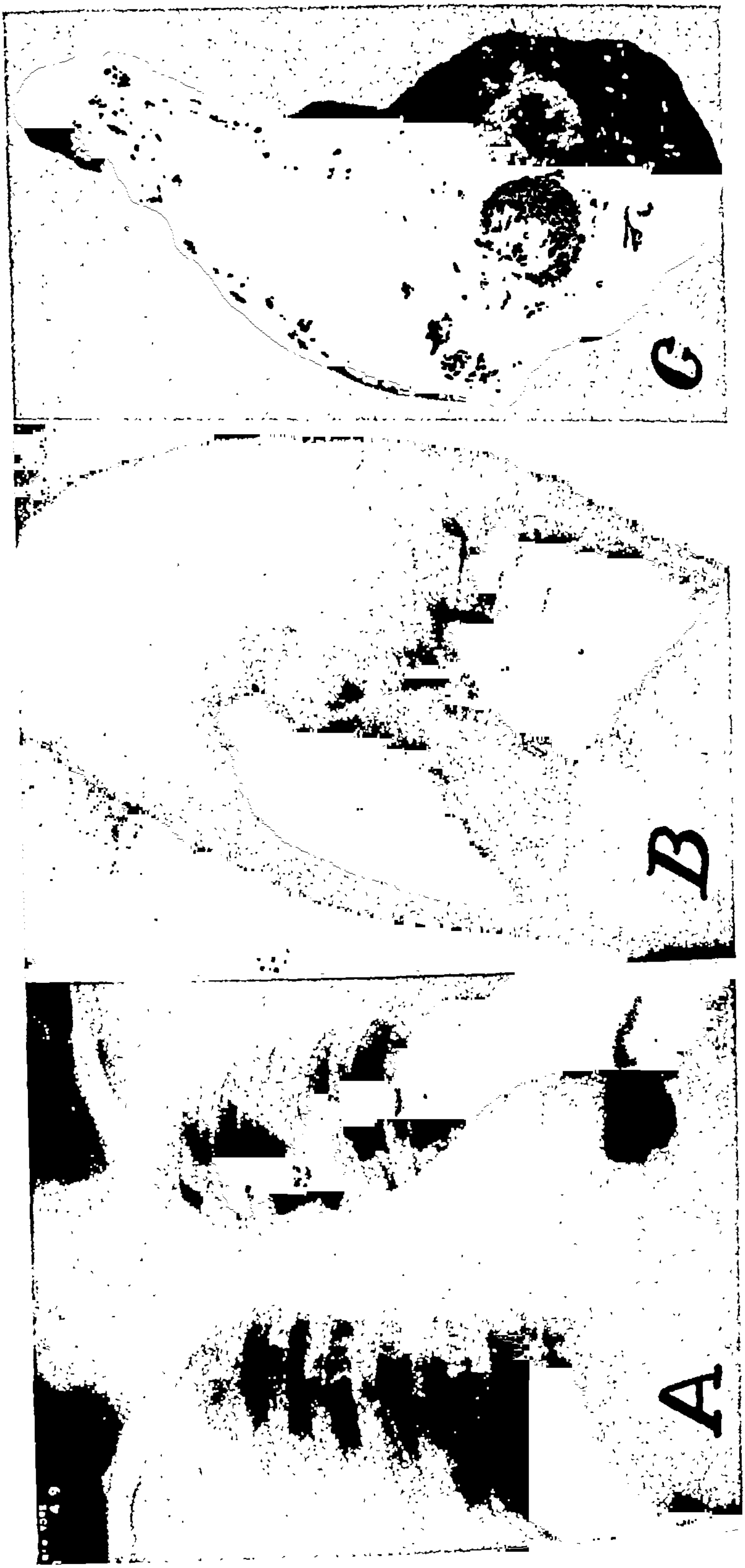

Fig. 5 (Case 5).—*A* and *B*, Rounded mass in left upper lobe. The outermost border of this lesion is indistinct and seems to infiltrate the pulmonary fields. There is an area of diminished density within the tumor mass.

C, Photograph of a resected lobe with tuberculoma transected.

Discussion.—There is no doubt that the preoperative diagnosis in this case should have been tuberculoma. Since this lesion was well calcified, and no area of radiolucency could be demonstrated in the tumor mass, it is now felt by this group that surgery was not indicated in this case. The procedure of choice should have been serial roentgenograms at periodic intervals. Patient is at present alive and well, and asymptomatic.

CASE 7.—A. McG., a 49-year-old woman, was hospitalized in January, 1945, because of a mass found in the pulmonary fields in a routine pre-employment examination of the chest. The patient was asymptomatic, and physical examination was negative.

A chest roentgenogram in January, 1945, demonstrated the presence of a solitary, circumscribed, roughly round shadow, 4 cm. in diameter, in the right middle lobe, close to the hilum. This mass was homogeneous in density. Linear calcification was noted along the lower border of the mass; there was also irregular flocculent calcification scattered throughout the mass. There was calcification in the hilar glands.

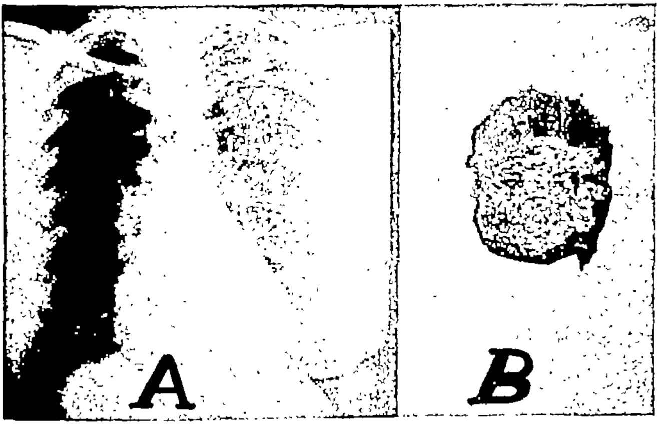

Fig. 6 (Case 6).—*A*, Roentgenogram shows a small lesion in the right lower lobe. There is a calcium deposit around the periphery of the lesion. Calcification can be seen in hilar glands and pulmonary fields.

B, Transected specimen.

Repeated bronchoscopic studies were negative. *Bacteriologic studies for tubercle* bacilli and fungi were negative. The patient was followed in the Out Patient Department until December, 1948. During this time there was no change in the mass.

On Dec. 12, 1948, when a thoracotomy was performed, a round cream-colored mass was found lying near the hilum of the right lung, half embedded in the parenchyma of the middle lobe. The mass was removed by separating it from the lung tissue.

The specimen was an encapsulated mass 4 cm. in diameter. On section, the tumor was yellowish white in coloration, very firm in consistency, with areas in which there was marked deposition of calcium. The tumor mass appeared to be largely fibrous, with fibers arranged in whorls. In occasional areas the tissue was relatively soft in consistency. The center of the lesion consisted of a conglomeration of old calcified and partly ossified tubercles. These calcified and ossified areas were separated by firmly hyalinized connective tissue which had resorbed part of the calcified periphery of these tubercles. The entire surrounding area was a firm, fibrous stroma comprising a few thin areas of original alveoli.

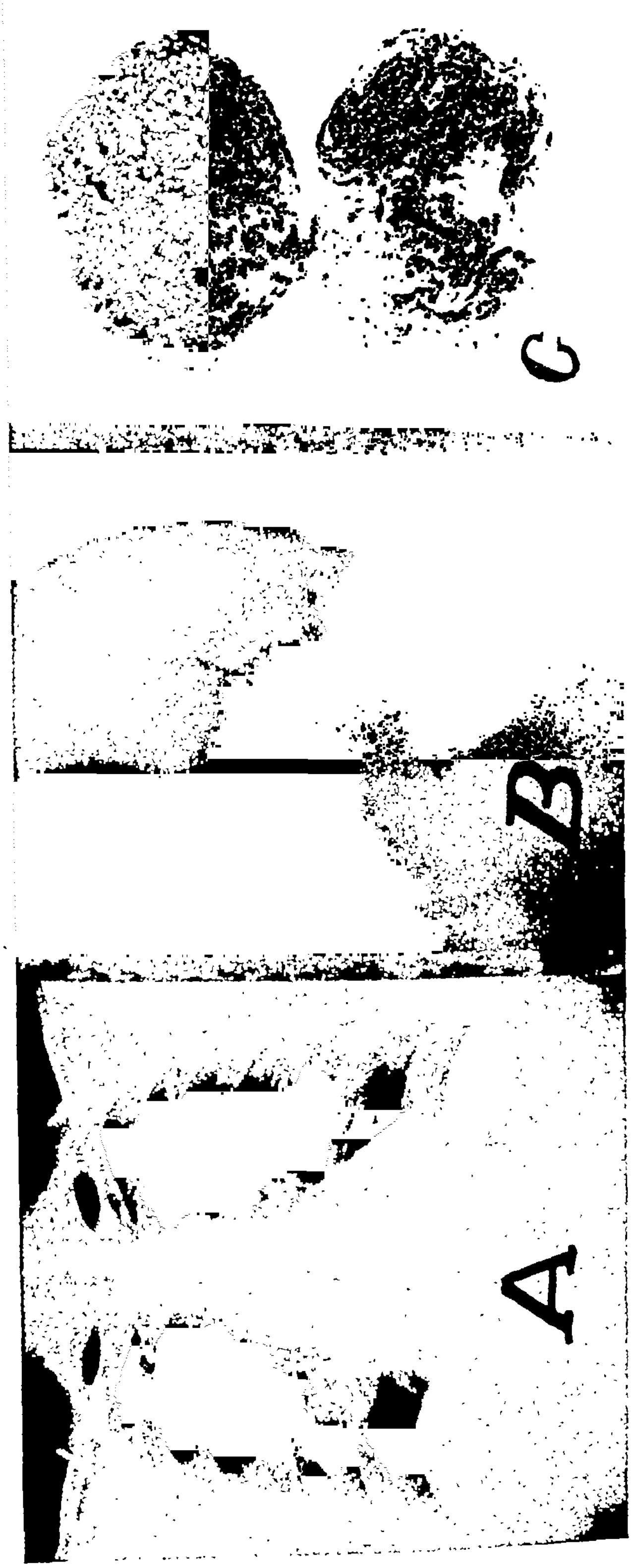

Fig. 7 (Case 7).—*A* and *B*, Posteroanterior and lateral roentgenograms show a circumscribed mass in the right middle lobe close to the hilum. Linear calcification can be noted in the lower border of the mass.

C, Photograph of enucleated tuberculoma.

The patient had an uneventful recovery, and was discharged Dec. 20, 1948. While at home she had a sudden onset of nausea, anorexia, shortness of breath on exertion, and on Jan. 29, 1949, was re-admitted. A right side empyema was discovered, and 300 c.c. of purulent material removed by needle from the chest. On Jan. 30, 1949, an open thoracotomy was done for drainage of the empyema pocket which extended from the apex down to the sixth rib. The empyema cavity was again explored, Feb. 10, 1949, culture of pus from the right chest was positive for tubercle bacilli. The patient improved after this. Roentgenograms showed the empyema cavity to be gradually decreasing in size. Despite the presence of a definite bronchopleural fistula, the wound was completely healed by June, and the patient has since been well.

Discussion.—This case presented a very difficult problem as to the method of treatment. Because there was only a moderate amount of calcification within the mass, a prediction as to the ultimate fate of the tumor could not be made. A thoracotomy was done for this reason. According to the criteria for operation, outlined later in this paper, the surgery in this case might have been deferred and observation continued.

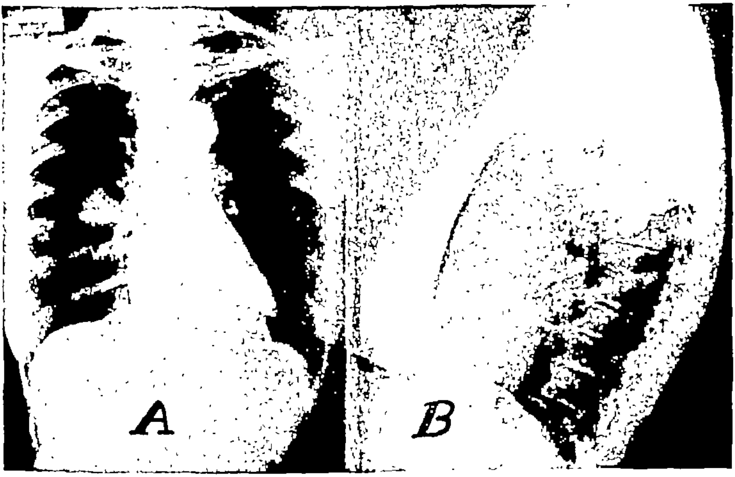

FIG. 8 (Case 8).—*A* and *B*, Roentgenogram shows a singular circular homogeneous density in the right lung, in the angle between the major and minor fissures at the hilum. Multiple areas of calcification are seen in the tumor mass, hilar glands, and lung fields.

CASE 8.—K. C., a 65-year-old woman, was seen in April, 1948, because of the discovery of a mass in the chest at a cancer detection clinic. The patient was asymptomatic, and physical examination was negative.

Roentgen examination of the chest showed a single circular homogeneous density 3 cm. in diameter in the right lung, in the angle between the major and minor fissures at the hilum. There were multiple scattered areas of calcification in the tumor mass, *hilar* glands, and lung fields.

Bronchoscopy was negative. Repeated sputa and gastric washings on direct and concentrated smears were negative for tubercle bacilli. Smear and cultures from bronchial

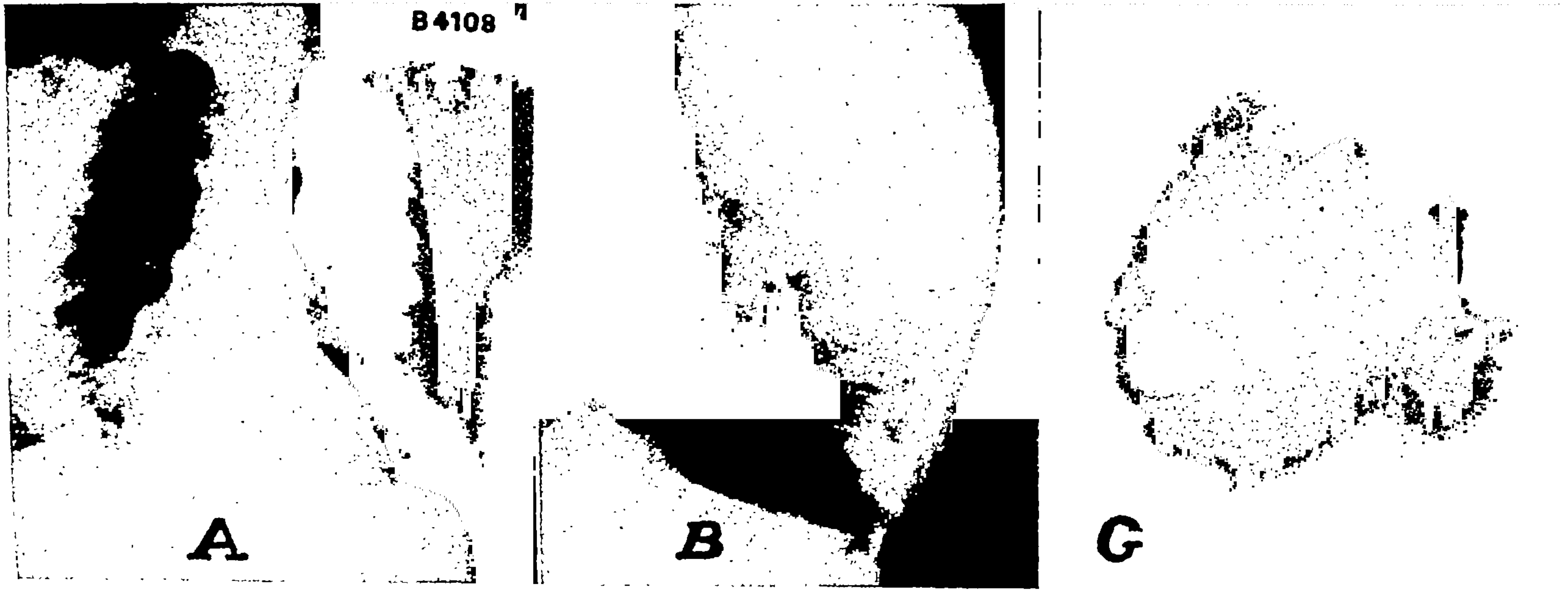

Fig. 9 (Case 9).—*A* and *B*, Roentgenograms in posteroanterior and lateral projections show two rounded lesions in the right lower lobe posteriorly. Calcification is seen in the lower border of the upper tuberculoma. Calcification is seen in hilar nodes.
C, Roentgenogram of resected lobe demonstrates that the tuberculoma contains a large amount of calcium.

aspirations were negative for acid-fast bacilli and fungi. Later cultures and guinea pig inoculations were both reported positive for tuberculosis.

Discussion.—Operation was deemed inadvisable because of the general condition of the patient, repeated negative bronchoscopies, lack of progression of the lesion, and position of the lesion which would have necessitated pneumonectomy. Last chest film was in January, 1950, The appearance was the same.

CASE 9.—C. W., a 54-year-old man, was hospitalized on Jan. 15, 1948. One month before admission he had noticed some shortness of breath on exertion. He had a cough productive of four tablespoons of sputum daily. He also developed a sharp pain in the anterior right chest which lasted one week. Physical examination was negative.

Roentgenographic examination of the chest revealed two rounded lesions in the right lower lobe posteriorly, each being slightly more than 1 inch in diameter, lying one above the other, one slightly anterior. These were round and circumscribed, and in such proximity to each other that they actually overlapped. Tomographic studies of these lesions demonstrated partial calcification in the wall of the superior lesion, and scattered areas of calcification throughout the tumor masses. There were discrete areas of calcification in the hilar nodes.

Bronchoscopy showed a moderate degree of chronic inflammatory reaction. There were no localized lesions in either the right or the left main bronchi, or in the secondary orifices. Bronchial secretions were negative for tubercle bacilli. Cultures were also negative.

On the ninth hospital day a right lobectomy was done. There was found to be an extremely hard white tumor within the substance of the lower lobe, which had the appearance of cartilage on the pleural surface. There were some hard nodes about the lower lobe hilum which were likewise calcified.

On section, there were two, golf-ball size, distinctly encapsulated tumor masses, apparently tuberculomas. One measured 2.8 cm. in diameter, and the other 2.5 cm. Section through the tuberculomas showed a fairly thick fibrous capsule, and extensive calcification of the caseous tissues. The surrounding alveoli were compressed and somewhat atelectatic. No active tuberculous granulative tissue was seen.

On the sixteenth day the patient was discharged with wounds well healed.

Discussion.—The presence of dense calcification in the tumor masses simplified and justified the diagnosis of pulmonary tuberculoma. This calcification was sufficient to be of prognostic significance. Surgery was probably not indicated at this time because of the apparent instability of the lesion as indicated by the amount of calcification within the tuberculoma. Roentgenographic examination of the chest at regular intervals might have been a wiser decision.

CASE 10.—D. N., a 74-year-old white man, was seen in March, 1948, because of an unusual finding in a routine chest film taken by his physician. The patient was asymptomatic on admission, and physical examination of the lungs was negative.

Roentgenographic examination revealed a roughly round tumor, 6 cm. in diameter, extending out from the mediastinum into the lung fields. Lateral film of this chest showed this lesion to be in the middle mediastinum. The mass had irregular borders and discrete areas of calcification. The rest of the lung fields were normal, except for scattered areas of calcification.

Bronchoscopic examination showed the carina to be moderately fixed. The right bronchus was not remarkable. The left bronchus seemed to be pushed anteriorly and upward, but all subdivisions could be recognized. Bacteriologic studies of sputa and bronchial aspirations were negative. Cultures and guinea pig inoculations were negative.

The thoracic surgical consultant felt, because of the bronchoscopic findings, that this case was most likely a lymphoma, and because of the patient's age recommended a therapeutic trial of roentgen therapy before subjecting him to an exploratory thoracotomy. The patient received intensive radiation treatment with no diminution of the size of the tumor.

On Aug. 10, 1948, an exploratory thoracotomy was done. Extending out from the mediastinum into the right upper lobe of the lung there was a mass the size of a small orange studded with calcified pebbles over its surface. It was extremely hard, yellow in color, and did not deform the lung. The operating surgeon felt that this was probably a tuberculoma because of its color, consistency, and surface appearance. Biopsy was not considered advisable. The tumor was not resected because of patient's age and poor general condition. Patient's postoperative course was uneventful.

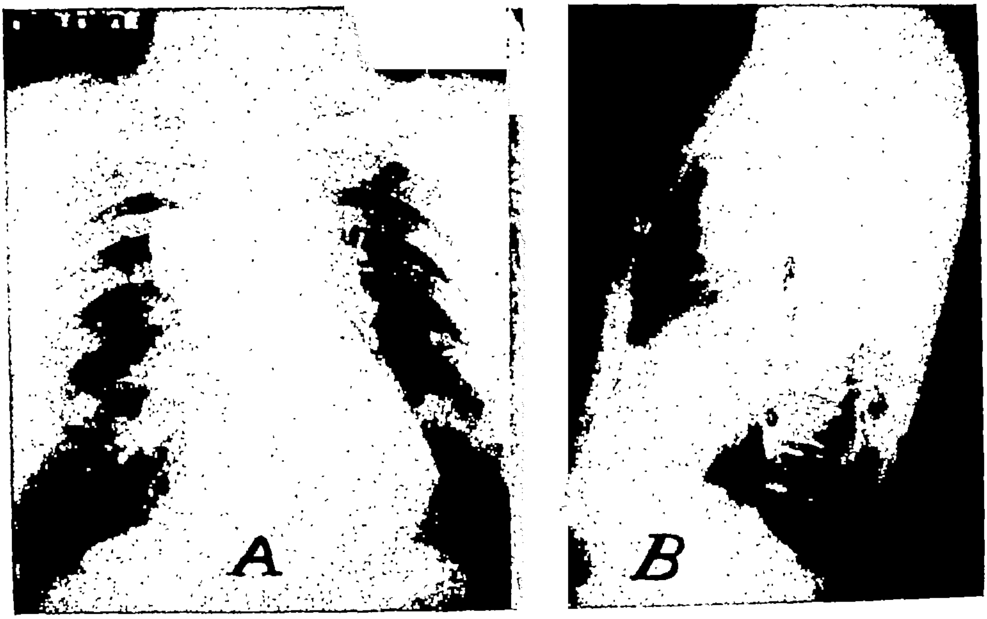

Fig. 10 (Case 10).—*A* and *B*, Roentgenograms in posteroanterior and lateral projections show a roughly round tumor 6 by 6 cm. extending out from the mediastinum into the lung fields. The mass has irregular borders and discrete areas of calcification. Scattered areas of calcification can be seen in the lung fields.

Case 11.—L. D., a 72-year-old Negro, was seen on June 19, 1946. One year previous to admission a chest plate had been taken, and a diagnosis of *mediastinal tumor with calcification* has been made. On admission to the hospital the patient's chief complaint was marked progressive dyspnea. He had a productive cough, without blood-streaking. At the age of 18 years, cervical tuberculous glands had been removed at the Johns Hopkins Hospital.

Physical Examination.—The patient was a cachectic, elderly Negro. The chest was emphysematous; dullness was elicited over the right interscapular area. Râles and rhonchi were heard in both apices. Remainder of examination was essentially negative. While in the hospital, patient had a daily low-grade fever.

Numerous roentgenograms of the chest were made. Examination of the chest and mediastinum in December, 1946, fluoroscopically and radiographically, showed a huge tumor mass with calcification in its wall. This mass was posterior to the trachea, in front of the spine, and extending to either side of the spine. The trachea was pushed far forward and the bifurcation of the trachea was pushed upward. Multiple areas of calcification were noted in the paratracheal and hilar nodes. Large areas of calcification could be noted in the upper abdomen. This mass was believed to be a posterior mediastinal tumor, with calcification in the wall. The following possibilities were considered: (1) echinococcic cyst; (2) huge tuberculoma with calcification in the wall; (3) nodular enlargement of the aberrant thyroid tissue with secondary calcification.

Repeat roentgenogram in June, 1948, showed infiltration in the right infraclavicular and apical areas, with what appeared to be multiple fine areas of cavitation.

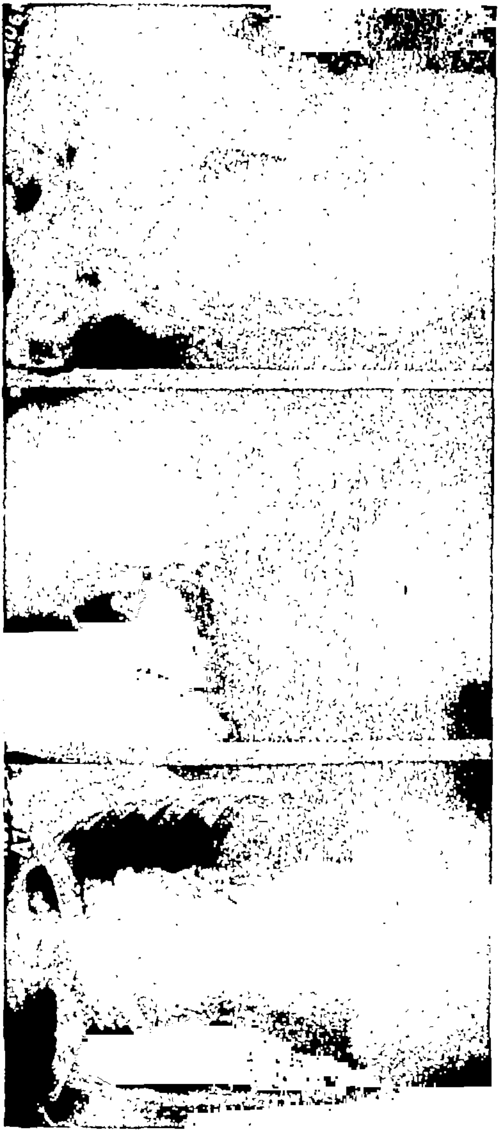

Fig. 11 (Case 11).—Roentgenograms in posteroanterior, lateral, and oblique projections showed a huge tumor mass with calcification in its wall. The trachea was pushed forward and the carina upward. Multiple areas of calcification are seen in the paratracheal and hilar nodes.

Re-examination of the chest on July 3, 1948, showed an increase in the infiltrative lesions, extending down into the right lower lobe from the hilum. There was a small amount of fluid at the costophrenic angle.

Repeat cultures and films were negative for tubercle bacilli.

Discussion.—Cases 10 and 11 are presented to illustrate tuberculomas of the mediastinum. Case 11, in view of the spreading infiltrative lesions in the right upper lobe, is probably a tuberculoma of the mediastinum, although pathological or surgical proof is lacking.

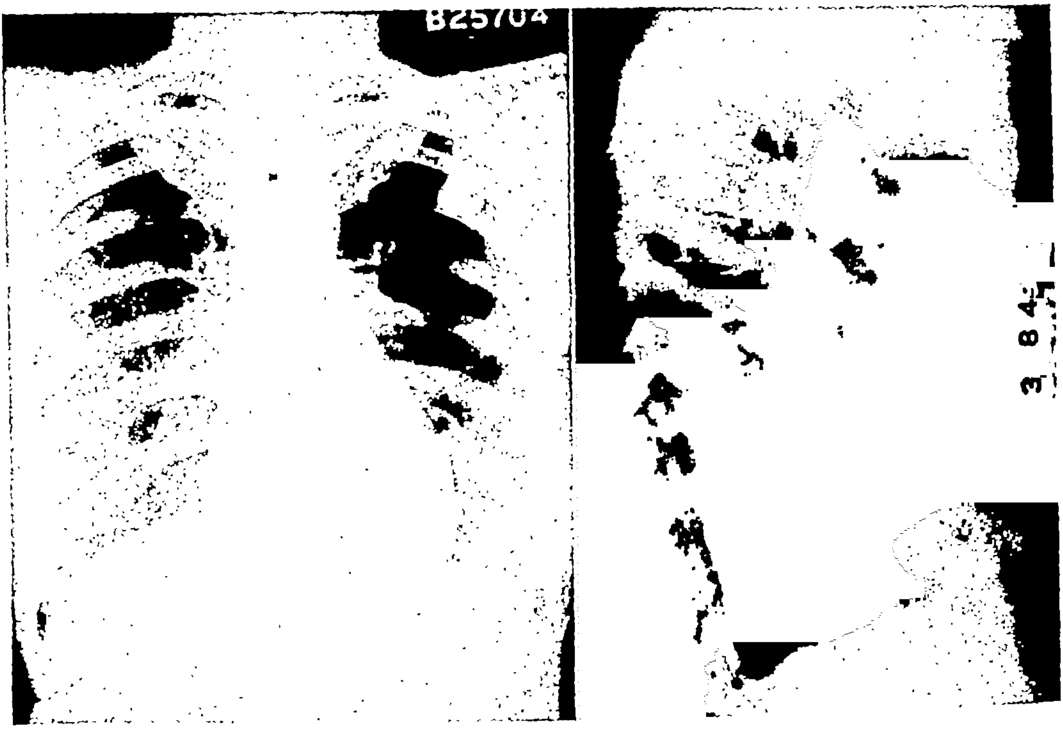

Fig 12.—This case was not presented in the body of the paper. It demonstrates very well two almost completely calcified tuberculomas in the left upper lobe.

MANAGEMENT

The radiographic demonstration of a solitary circumscribed lesion without calcification in the lung fields, in which all other diagnostic studies are negative, demands an exploratory thoracotomy. It is a relatively safe procedure, and has a low mortality and morbidity rate. Since many of these tumors will be malignant, exploration as soon as possible is the treatment of choice. Should the lesion prove to be metastatic, recent reports[25] have indicated that resection of isolated metastatic tumors in the lung fields may be beneficial, particularly if the primary lesion has been eradicated. A large number of these solitary tumors will prove to be of tuberculous origin. There is increasing evidence that resection of localized tuberculous lesions of this type is advisable.

The position of the mass may make the surgical management simple or complicated. The mass, if in peripheral location, may allow easy examination at operation, and, should a tuberculoma or other non-neoplastic process be present, local resection is feasible and safe. When the lesion is located at the hilum and is not calcified, the matter is much more serious, for, since the majority of such cases will be malignant tumors, we have no alternative but exploration with the idea of pneumonectomy. It is doubtful if sharp local excision of a suspected tuberculoma at the hilum of the lung is good practice. When a local resection of a tuberculoma in the hilar region is done, numerous fine bronchi are opened, whose fluid and air contents are difficult to control. These bronchial contents pass out into the field and invariably contaminate the operative area, increasing the likelihood of a combined infection which may have disastrous consequences for the patient. The one case in this series in which local excision of a hilar tuberculoma was done was complicated by a postoperative mixed empyema and bronchopleural fistula. Therefore, it must be anticipated before surgery that, if the mass is hilar, the surgeon may have to sacrifice the lung, even in the absence of neoplastic disease, since there is often little room for the safe application of less radical measures. Biopsies of these hilar masses are not always safe if the pathologist reports the presence of a chronic granuloma. A peripheral location of the lesion allows more conservatism, if the operator is in doubt, and therefore a greater margin of safety and less physiologic sacrifice for the patient.

The unchanged appearance of the mass in serial roentgenograms over a few months is not convincing evidence that the lesion is benign, as it is precisely this type of slowly growing neoplasm which is often the most favorable for resection and cure. If a tuberculoma can be removed with a wide margin of normal lung by means of a conservative operation, no particular harm has been done. A peripheral lesion without a definite diagnosis demands an exploration. If there seems to be doubt as to the nature of the lesion, and a biopsy does not seem wise, a pneumonectomy should be performed, if sufficient respiratory reserve exists. Should the lesion lie at the hilar region, and ablation by lobectomy is not feasible, and we have the choice of teasing out the the mass from the hilar structures, or pneumonectomy, the latter is probably preferable, although there may be individual factors which would direct the procedure otherwise in selected cases.

Well-calcified tuberculomas without areas of breakdown can probably be considered stable, and it does not seem to the authors that surgical intervention is the best method of management. The incidence of postoperative complications when added to the mortality rate of pneumonectomy, lobectomy, or local excision probably makes operation more hazardous than conservatism in this type of case.

Further observations over a number of years on carefully selected cases must be carried out before the preceding statements can be fully substantiated. However, it is only by this method that we can with reasonable certainty select the proper treatment for each patient.

CONCLUSIONS

1. Tuberculomas may arise from encapsulation of a primary giant tuberculous focus, from encapsulation of a restricted reinfection focus, or by means of a completely blocked tuberculous cavity.

2. The accurate differential diagnosis of a solitary mass within the lung fields may be extremely difficult or impossible, and in a large number of cases an exploratory thoracotomy will be necessary to establish the correct diagnosis.
3. Tuberculomas without calcification, or with areas of breakdown, constitute a potent threat against the continued well-being of the patient, and should be removed.
4. It is probably safe to advise conservative, well-managed observation in patients presenting definitely calcified solitary lesions without any evident breakdown.

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DISCUSSION

COL. JAMES H. FORSEE, Denver.—Added emphasis to the surgical management of tuberculosis may be given by reporting an experience we have had at Fitzsimons in the surgical management of sixty patients with tuberculoma. Approximately two-thirds of the patients have been handled surgically by wedge excision of the lesion, one-third by lobectomy. We believe this is an actual and potentially dangerous lesion and, in general, that all tuberculomas should be removed by surgical means. True, certain patients who have had for many years known tuberculous lesions, may be treated conservatively.

(Slide.) This illustrates a typical tuberculoma.

(Slide.) This is a surgical specimen—what we call a mature tuberculoma; here is a colored photograph of that specimen.

(Slide.) There is no means with which we are acquainted by which we can tell preoperatively and without examination of pathologic tissue, the true nature of the lesion in most instances. This lesion, as you will note, is circumscribed; it may or may not be a mature lesion; we cannot tell by x-ray findings.

(Slide.) This is the surgical specimen—it is an unripe lesion teeming with tubercle bacilli. The wedge excision which we performed is, as you see, too small for this type of lesion, and had we known beforehand we would have removed more parenchymal tissue.

(Slide.) There is an area of translucency near the border of this circumscribed lesion, which our pathologist, Colonel Mahon, has pointed out occurs in a certain percentage of cases, indicating a break-through of the encapsulated lesion, and we believe it is a definite indication for consideration for surgical excision.

(Slide.) This film again shows a typical tuberculoma, but impossible to tell by roentgenographic examination. This patient did have symptoms of mild fever.

(Slide.) This is the surgical specimen of a lobectomy; the patient had a cavitary lesion, a breakdown of the tuberculoma, and endobronchial disease.

(Slide.) The danger of tuberculoma is well illustrated in this particular instance; a 36-year-old woman who had been watched for seven years. She had been advised to have exploration of this lesion in 1945 in the midst of the war, and she deferred exploration. We saw her in 1947; the tuberculoma had broken down and she had had dissemination of the disease.

In general, calcification takes a long time to develop. Streptomycin has no effect on these lesions and we believe surgical exploration and excision is the proper therapy.

DR. JOHN R. PAINE, Buffalo.—Dr. Culver and I come from the same clinic. Before we get too far out on a limb, I want to say that I personally subscribe to the management expressed by him which, briefly, is this: we think all tuberculomas should be excised except those that are calcified with no evidence of internal breakdown. However, even in that class of patient, we think they should be followed with serial x-ray films every three months. If at any time they do show internal breakdown or radiotranslucency, we think they should be excised.

(Slides.) Dr. Culver's series is twenty-three; this will be his twenty-fourth. This is the last case which has come to our attention. This is the x-ray film of a 51-year-old woman who is asymptomatic; this was a survey film taken last October. We have spent since last November until the *first of April trying* to find out where the primary tumor was in this case. There are twelve distinct lesions in this woman's x-ray film. On close scrutiny of the original film seven of these lesions showed calcification. Has she got multple tuberculomas? Has she got metastatic carcinoma? We have spent about four months trying to find where the primary tumor might be. Two weeks ago we excised one of these lesions for biopsy.

(Slide.) This proved to be a mature tuberculoma. While it is true that multiple tuberculomas do not occur very frequently, there are three out of the twenty-four. I think these multiple lesions occasionally cause a good deal of doubt as to how they should be treated properly.

DR. EDGAR DAVIS, Washington, D. C.—Several years ago before this Association I discussed a paper on intrapulmonary tumors—I do not recall by whom the paper was given. For a number of years we have been much interested in these solitary tumors. In the original forty cases which I presented, we had a total of 70 per cent malignant and 30 per cent benign lesions. No tumor was included which showed any evidence of excavation or calcium; nor were tumors included that were located against the diaphragm, the chest wall, or the mediastinum. The average age of the forty patients was 52 years. At that time it was predicted that if a chest x-ray survey could be made whereby a large group of the younger people could be studied, the percentage of malignancies would diminish and there would be a corresponding increase in the so-called tuberculomas. In 1948, a mass chest x-ray survey was carried out in Washington, D. C., at which time about one-half million people above the age of 14 years were x-rayed. We have now accumulated, partly from that mass chest x-ray survey and partly from other sources, a series of 92 or 93 of these solitary tumors. Sixty-seven of these cases have been completely tabulated, of which 55 per cent were malignant. The remaining 25 or 26 cases, although not completely analyzed, are showing approximately the same results. It is interesting to note that of the patients who had no symptoms whatever referable to the chest, 28 per cent were found to be malignant. Although this may be considered a relatively small series, it is sufficient, in my opinion, to justify immediate action and early removal rather than watchful waiting.

DR. W. O. KELLEY, Norwich, Conn.—I agree with Dr. Culver's discussion on the pathogenesis of tuberculoma generally. However, I would like to make the statement that there may be some disagreement as to whether we should actually classify as tuberculomas the formation of an intrapulmonary cavity and later the filling of this cavity with secretion. On the other hand, in tuberculoma, if we can follow the progress, we actually see first a solid tumor, later breaking down to form sometimes a fairly large cavity. To illustrate this I have three cases that could be added to this series.

(Slide.) This is the case of a 23-year-old woman who had three masses, one small, one of medium size, and one large. The patient had a positive sputum which continued positive in spite of pneumothorax treatment.

(Slide.) In the lower mass, the largest one, there is definite rarefaction.

(Slide.) This is the removal of the upper lobe, with an incision made vertically on the apex to the base, showing the first, the second, and the third mass with cavity formation.

(Slide.) This is an x-ray film of another case in which we have proof that there was a tuberculoma; there is probably some breaking down but it does not show clearly here.

(Slide.) The laminagram shows the mass a little more clearly.

(Slide.) This is the resected upper lobe, and here is the tuberculoma in section, one-half here, and one-half here.

(Slide.) Another case with a mass under the right clavicle.

(Slide.) Here is perhaps what we would call a ripened or mature tuberculoma in cross section.

(Slide.) This is the result postoperatively.

DR. DEWITT C. DAUGHTRY, Miami.—This is a very interesting topic. I have recently seen several cases that were of great interest, at least to me. One of these lesions was indistinguishable from a tuberculoma and broke down in a few weeks to produce a disseminated histoplasmosis. Another one was a dense round lesion which was excised, and was a granuloma due to localized blastomycosis. The majority of these lesions that I have seen have proved to be carcinoma. Some of them had not changed in size in two or three years' time. I would like to show one case to demonstrate what may happen to a tuberculoma which had changed very little in five years.

(Slide.) This lesion was present five years ago, *asymptomatic*, and had not changed until about three months before this film was taken. The patient became symptomatic, had a negative sputum, did not feel well, but did have a cough. The lingula containing the lesion was resected.

(Slide.) This shows that it is a granulomatous tuberculous lesion which has broken down, in spite of the fact that it had apparently been stable for five years.

Seldom can a definite diagnosis be made when we visualize a discrete round solid peripheral opacity on the x-ray film. These lesions must be considered very dangerous, and we should not feel content until we have them in a specimen jar.

DR. W. M. TUTTLE, Detroit.—I do not believe that there is any doubt in the minds of most of us present but what the rounded lesion within the lung should be surgically removed. There is on the other hand a considerable danger because of the fact that many individuals in the field of medicine have come to believe that the rounded lesion is a relatively benign process. The idea is all too current that the rounded lesion can be safely watched, if it does not over a period of months demonstrate growth then it is considered either an inflammatory process or some benign tumor, if it grows then it is considered naturally to be malignant. This, of course, is an absolutely inaccurate view of the facts. There are numerous carcinomas which grow slowly, if at all, over a period of many months. I have recently seen such a lesion in a woman of middle age which was watched for a period of approximately eight months in which no growth was demonstrated. Six months after this watching period she returned with a lesion many times the size of the original one. A pulmonary resection was done and it was evident that the mediastinal glands were involved. The mere fact that an area of calcification is present within the center of the rounded lesion is no proof that the lesion is tuberculous rather than benign. We have recently resected such a lesion in which a carcinoma had developed about a previous Ghon's tubercle. In view of many recent studies which demonstrate that the rounded lesion within the lung carried an incidence of malignancy in from 25 to 50 per cent of the patients seen with this type of lesion it is certainly unsafe to temporize.

DR. JOHN R. MC DONALD, Rochester, Minn.—In a surgical pathological laboratory, between twenty and thirty varying surgical conditions are seen for which resective pulmonary operations are performed. One of the largest groups results from granulomas, there being a great variety that affect the lung. These granulomas may be produced by bacteria, molds, parasites, or chemicals. The histologic pattern is often similar regardless of etiological factors. Too often an opinion is given that a certain granuloma is caused by *Mycobacterium tuberculosis* without any adequate bacteriologic proof. To me it seems unwise to diagnose a given granuloma of the lung as a tuberculoma without this proof.

DR. NORMAN WILSON, Brookline, Mass.—I rise to ask Dr. Culver if he would be kind enough in his closing discussion to tell us from his experience and study, what cases he thinks we should treat as tuberculous patients after the excision. This problem was brought to my mind forcibly by two successive cases which I recently have done, both survey lesions, both having isolated round tuberculomas in the lung tissue, with nothing else seen by x-ray examination or palpation, but with large hilar nodes which looked to be active. I wondered whether he had had this experience, and which patients he felt should be admitted to the sanatorium for treatment.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—I certainly agree with Dr. Tuttle that these rounded tumors, when they are found, should be surgically attacked if there are no special contraindications to operation. I should like to discuss the type of attack that we plan in these cases. Nobody can tell from the x-ray film the microscopic pathology in these tumors. When we explore them, we always make on the table a frozen section from the area of the tumor in order to ascertain what type of pathology is present. If it is a malignant tumor we prefer routinely to do pneumonectomy; only in selected cases where there is good reason for it, lobectomy is done. In the cases where we find it is a benign process, and if this is well localized, we prefer to dissect the pulmonary artery and the main stem of the two veins. We clamp these vessels temporarily. We dissect the bronchus with the bronchial arteries and clamp these as well. We thus get a bloodless field in which we proceed to do a local open excision of the benign process. We pick up and ligate the vessels which are at the bottom of the cavity. We also ligate smaller bronchial luminae, after larger bronchial defects are sutured, until we have a bloodless field free from air leak also after the clamps are released. The cavity is closed by a few sutures and the chest wall is closed. In suitable cases segmental resection is performed.

DR. CULVER (closing).—It seems necessary to stress the fact that our management of the usual solitary round intrapulmonary lesion is at no variance with the opinions offered by the discussors, as was stated in the body of the paper. Neither do we have any misconception that lack of growth in such a lesion in any way rules out malignancy.

Our main thought has been to stress the point that calcification does not occur in primary pulmonary malignancies.

A tumor without calcification is treated in the accepted manner. It is the calcified lesion without evident breakdown that we treat conservatively. In the older age group, in individuals with diminished respiratory reserve, this conservative management probably is best applied. We feel that the incidence of postoperative complications, when added to the mortality rate of pneumonectomy, lobectomy or local excision, probably makes operation more hazardous than conservatism in this type of case.

This is admittedly a recent survey; however, up to the present time we have encountered no complications in the cases followed. Certainly longer follow-ups will be necessary for final evaluation.

THE HEALING OF SURGICAL WOUNDS OF THE LUNG WITH PARTICULAR REFERENCE TO SEGMENTAL LOBECTOMY

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RESECTION of anatomic segments of pulmonary lobes has become a well-established surgical procedure.[3, 4, 8, 9, 10, 12] The earlier technical reports emphasized closure of the remaining lung defect, usually by a continuous suture.[4, 8] More recently, it has been recommended to leave the raw pulmonary surface as it presents itself following segmental excision.[8-11, 13] With the avoidance of suturing, it was believed that less distortion of the parenchyma resulted, and that better pulmonary function was maintained.

A disturbing feature of this operation is that most surgeons have had a higher postoperative morbidity than after total lobectomies. More complications have occurred no matter how the raw surface of the remaining lobar segment was treated.[2, 6, 10] The causes of the varied types of complications were not always clear, but many authors suspected that the unpleuralized lung surface was the source of trouble.

The fate of the residual lobar parenchyma has been conjectured, but no one has proposed a concept based on direct observation. This is due to scanty autopsy material since the mortality of these cases is low. It also has been rare for a surgeon to examine the results of a segmental lobectomy at a subsequent operation.

The following investigation was performed to determine the sequence of pathologic events in the healing of a parenchymal wound following the removal of an anatomic segment of lung. In most instances a block excision of an adjacent lobe without regard for intersegmental planes was also performed for comparison.

METHOD

Large adult cats were chosen for this study. After nembutal narcosis, a small catheter was inserted into the trachea and ether anesthesia was started. The pleural cavity was entered through the seventh intercostal space. In most instances the apical segment of the lower lobe of the right lung was chosen for resection.

The pulmonary lobes always had complete fissures. The apical bronchus of the lower lobe was identified and isolated for a short distance. A fine silk suture was tied about it

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From the Department of Surgery, Columbia University.

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close to the stem bronchus to the lower lobe. The bronchus was divided between this tie and a clamp placed distally. With slight traction on the clamp, the segmental vein and artery were readily seen and divided between ligatures. The intersegmental plane was identified with gentle blunt dissection near the clamped bronchial end, and the segment was removed with continuance of this technique. This maneuver was performed with ease and no troublesome bleeding from intersegmental veins was encountered. The resultant defect was usually smooth surfaced and measured approximately 2 by 1.5 by 1.5 cm. There was practically no capillary ooze from the surface, and alveolar leaks were either transient or absent. Increased intratracheal pressure demonstrated usually an airtight pulmonary wound. No attempt was made to pleuralize the defect.

The middle lobe was rotated into the wound and its tip was amputated with scissors. Bleeding ceased after the application of warm moist pads for several minutes. At first, the operation was terminated leaving this lesion unsutured. However, one animal died of empyema and a bronchopleural fistula from this defect. In subsequent cases, therefore, the cut end of bronchus was closed with a single mattress suture of fine silk. In most of these animals, the healing progress of a small parietal pleural wound also was studied and the findings will be reported later. The chest wall was closed in layers with silk about a small catheter. Near the end of operation, as much air as possible was aspirated from the chest through the catheter which was then removed. No dressings were applied and the animal was returned to its cage.

The postoperative recoveries were usually uneventful. No roentgenograms of the chest were taken and no thoracenteses were done. None of the animals in this series showed signs or symptoms of infection and all appeared healthy at the time of sacrifice. They were given lethal doses of ether at intervals from two days to six weeks after surgery. The abdomen was opened, and after the viscera were examined, they were retracted caudad. The pleural cavity on the operated side was first entered through an anterior diaphragmatic incision. In this manner the amount of residual pneumothorax could be evaluated easily. When this was determined the anterior chest wall was removed en bloc so that all the thoracic structures could be viewed in situ. With gentle manipulation of the wounded lung, pleural adhesions, the state of the wound, and possible pulmonary distortion were noted.

The lungs were removed and inflated with Bouin's solution via the main bronchi. The specimens were placed in this solution following ligation of the bronchi. Sections were taken from normal and wounded parts of the lungs. These were prepared with hematoxylin and eosin and Masson's trichrom stains.

RESULTS

Gross.—Most animals killed within the first six days after operation had minimal pneumothoraces. One cat was sacrificed on the second day because of moderate respiratory embarrassment. It had a marked bilateral pneumothorax that was caused by a leak from the cut end of the middle lobe branch bronchus. In this instance, the bronchial suture did not prevent a bronchopleural fistula.

Postoperative pleural effusions were not remarkable. There were small amounts of serosanguineous fluid in the costophrenic angles during the first five days. Even this was not observed later except in the cat killed at the end of three weeks. The pleura was always smooth and glistening.

One of the animals killed on the second day had fibrinous adhesions between the middle lobe defect of the right lung and the adjacent pericardium. The wound of the segmental resection of the right lower lobe remained free from adhesions until the sixth postoperative day. During the subsequent period it usually became adherent to the overlying upper lobe or to the pleural scar of the chest wall incision. The density of adhesions varied. When there was symphysis of the defect and the upper lobe, no attempt was made to separate them and both lobes were included in the sections. At no time was there gross distortion of the lung.

The middle lobe defect following amputation of its tip was puckered by the placement of the peribronchial suture. It was difficult, therefore, to determine its dimensions accurately. Precise measurements of the lower lobe segmental lesion could be made unless it was firmly adherent to adjacent structures. It did not show any change in size until the ninth day when it began to contract progressively. By the third week the center of the wound was depressed and its borders were elevated and rounded. The segmental lesion was covered by a thin layer of blood clot up to the third postoperative day. From the fourth to the seventh day, it was overspread with a film of fibrin. Thereafter, the surface had fibrous characteristics.

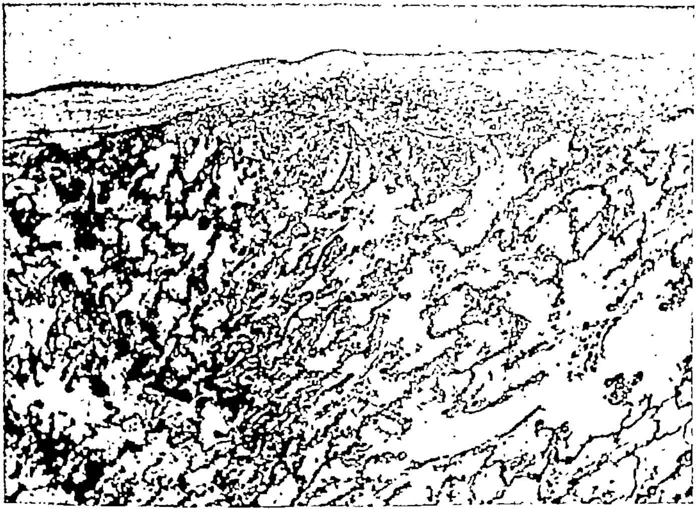

Fig. 1.—Wound of lung two days after segmental lobectomy. Note partial aeration of alveoli and increased caliber of capillaries (×130).

Microscopic.—The sections taken from the cat killed on the second postoperative day were the earliest studied by microscopy. The upper lobe of the right lung and lower lobe of the left lung showed evidence of patchy atelectasis. The bronchi in the involved sections contained considerable amounts of exudate. The segmental lesion of the lower lobe of the right lung was covered with a thin layer of blood clot (Fig. 1). The air sacs subjacent to it were aerated but smaller than elsewhere. In most places septal walls formed the border of the wound. Inflammatory cells near the injury were few and polymorphonuclear leucocytes were absent. The bronchi in these sections were free from blood, exudate, and retained secretion.

Sections from the cat killed three days after operation showed all pulmonary lobes to be well aerated. The segmental lesion was overspread by laminated strands of fibrin with intervening red blood cells in rouleaux (Fig. 2). Again there was a paucity of inflammatory cells. In one portion of the wound, there was evidence that the intersegmental plane was transgressed with resultant hemorrhage into the parenchyma and attenuated alveolar capillaries. This suggested a diminished blood flow through the area. The sections of this lesion showed air in all the alveoli, but there was pulmonary edema near the wound.

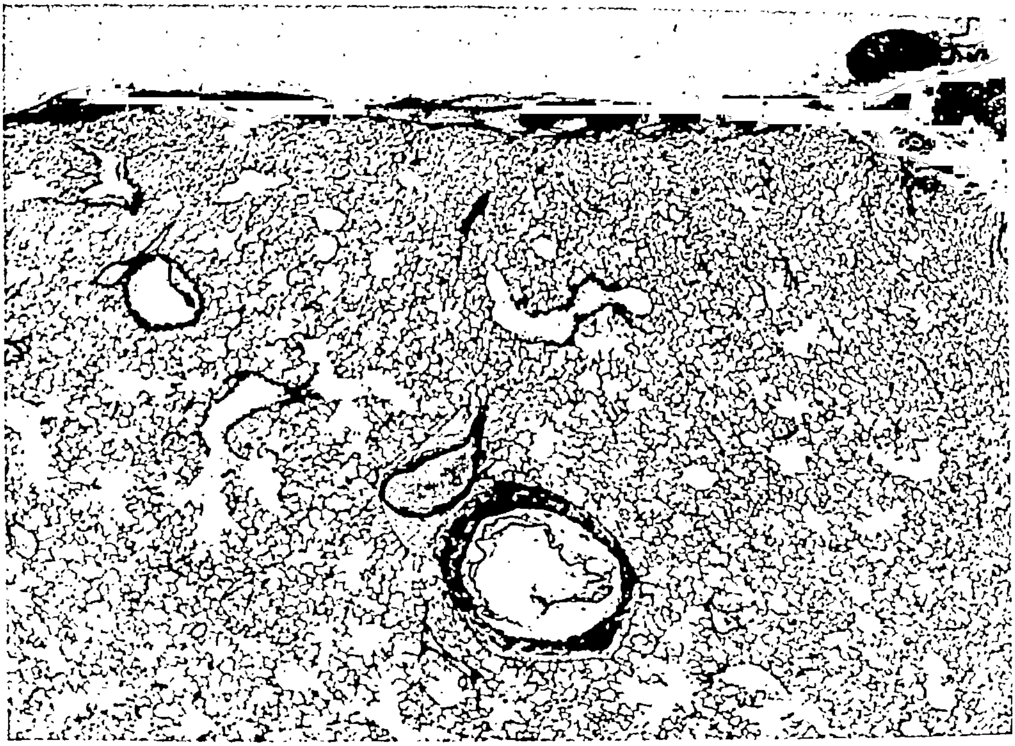

Fig. 2.—Segmental wound three days after operation. At the right the intersegmental plane was crossed, causing hemorrhage into the parenchyma locally. The remainder of the lobe is well aerated. There is pulmonary edema, especially near the wound (×18).

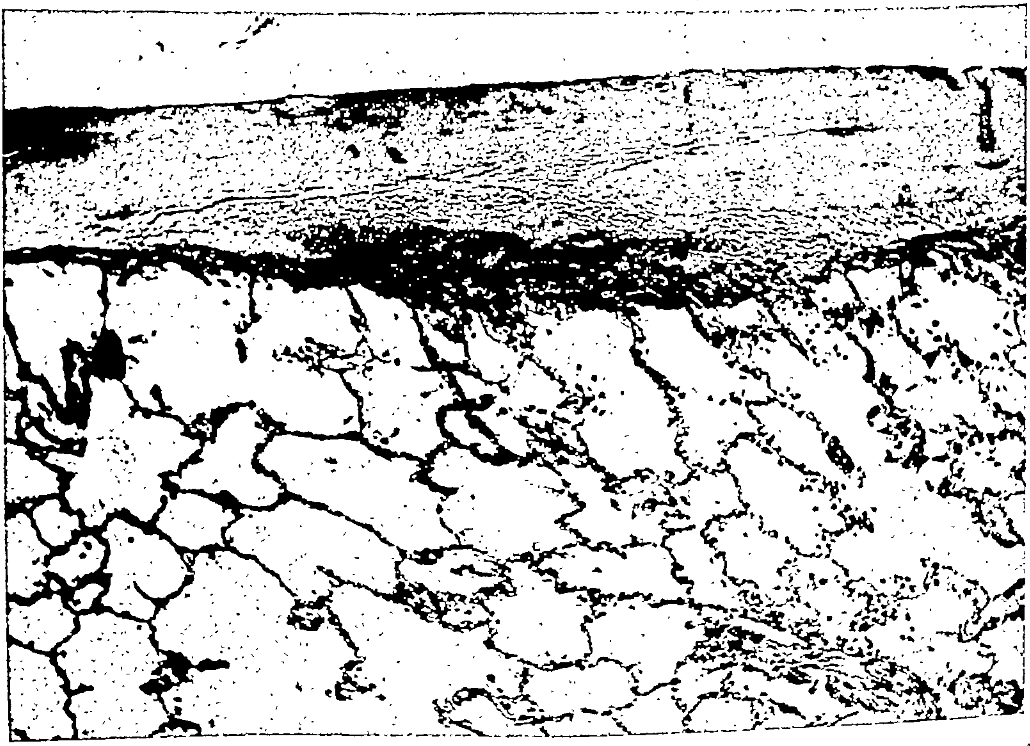

Fig. 3.—Segmental wound four days after operation. Pulmonary aeration adjacent to the wound is more complete. The lung border of the wound is formed by alveolar walls (×139).

During the next two days definite trends occurred. The partially excised lobes showed pulmonary edema. The lungs were well aerated except the middle and lower lobes on the right which had patchy areas of atelectasis, especially near the lesions. On the fifth day, the segmental wound was covered by a fibrinous layer containing disintegrating red blood cells. The layer was much thicker than noted on the previous days and it extended for a considerable distance over the adjacent pleura. Only directly over the wound did it contain all types of inflammatory cells in moderate numbers. Fibroblasts from the wounded lung invaded the fibrin in a patchy manner. Aeration of the underlying lung was variable in different sections but it was never completely atelectatic. The alveolar lining cells near the lesion were large and prominent. A bronchus in this lobe contained exudate.

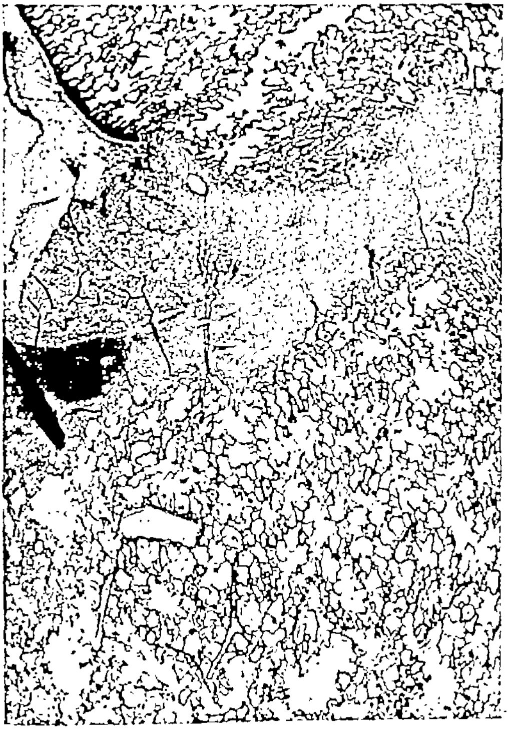

Fig. 4.—Segmental wound six days postoperatively. The wounded lobe in the lower one-half of the picture is adherent to the upper lobe by fibrinous agglutination. The wound is covered by a fibrotic layer (X31). (See text.)

The sixth day segmental wound was agglutinated by fibrin to the adjacent upper lobe (Fig. 4). The wound was covered with a layer of fibroblasts that paralleled its surface, but they did not extend to the adherent pleura of the upper lobe. Inflammatory cells were rare. Although the parenchyma showed normal aeration, some alveoli contained edema fluid. The bronchi in all sections were clean.

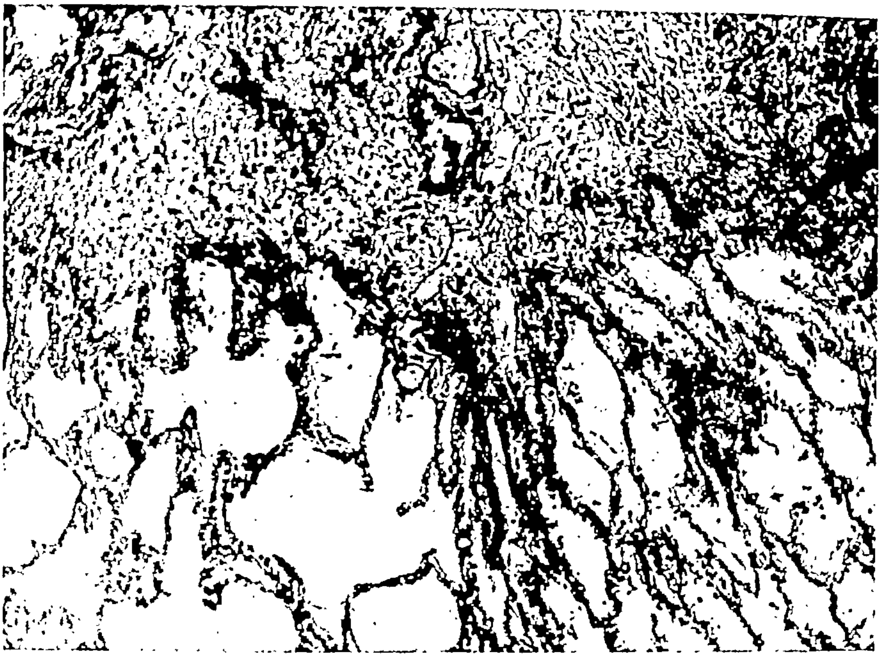

Fig. 5.—Segmental wound eleven days after operation. Note fibroblastic invasion of the fibrin layer and capillaries in the wound (×130).

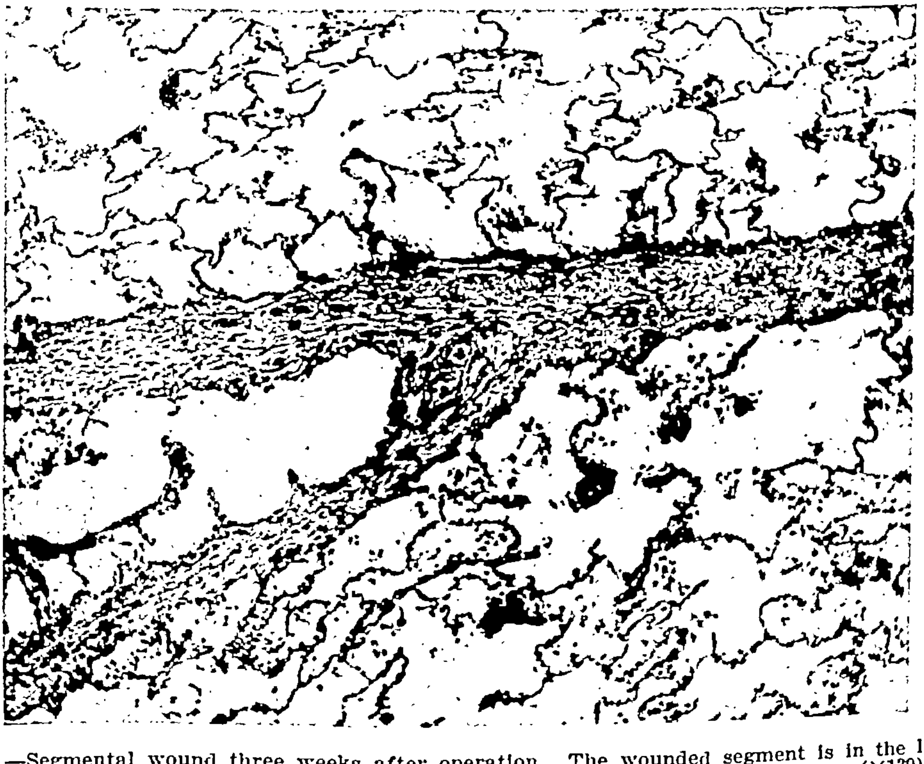

Fig. 6.—Segmental wound three weeks after operation. The wounded segment is in the lower one-half of the picture. Fibrosis has extended along the interlobular septum (×130).

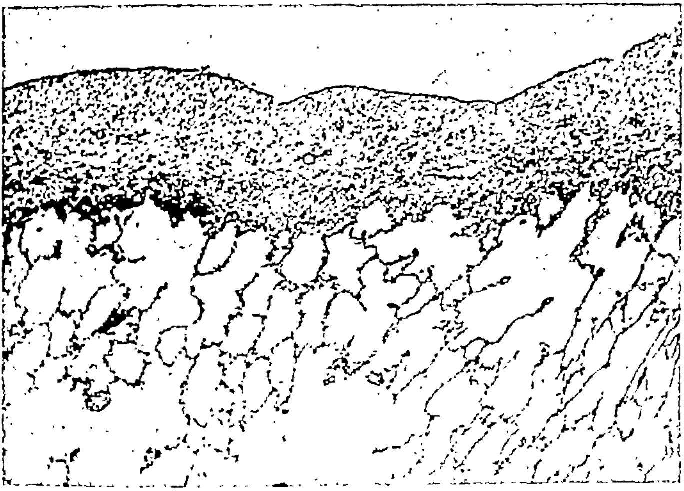

Fig. 7.—Segmental wound six weeks after operation. The scar is mature, undergoing hyalinization, and it contains numerous capillaries. The surface is covered by a single layer of cells (×139).

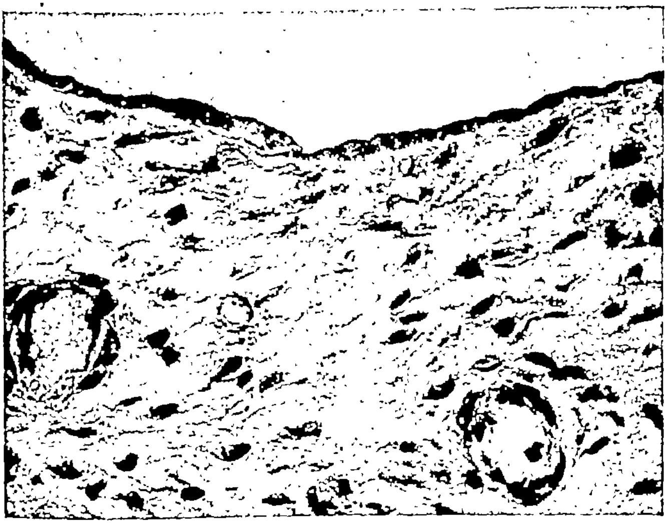

Fig. 8.—Higher magnification of Fig. 7 to demonstrate the cells on the wound surface (×1,064).

There was little noteworthy change until the *ninth* postoperative day. All lobes were fully expanded. The nonadherent portion of the segmental wound was overlaid with acellular fibrin that was completely enveloped by dense fibrous tissue. The bronchus to the remaining segment was damaged by suture so that the state of the parenchyma was not comparable to previous sections.

The next animal was killed on the eleventh day. There was a fibrotic symphysis of the segmental lesion and overlying upper lobe. A few clumps of fibrin were enmeshed in the adhesion but these were being invaded by fibroblasts (Fig. 5). Inflammatory reaction was minimal and the fibrotic area was well vascularized. The parenchymal pattern adjacent to the wound was slightly irregular but well aerated. The bronchi contained moderate amounts of exudate and there was peribronchial edema.

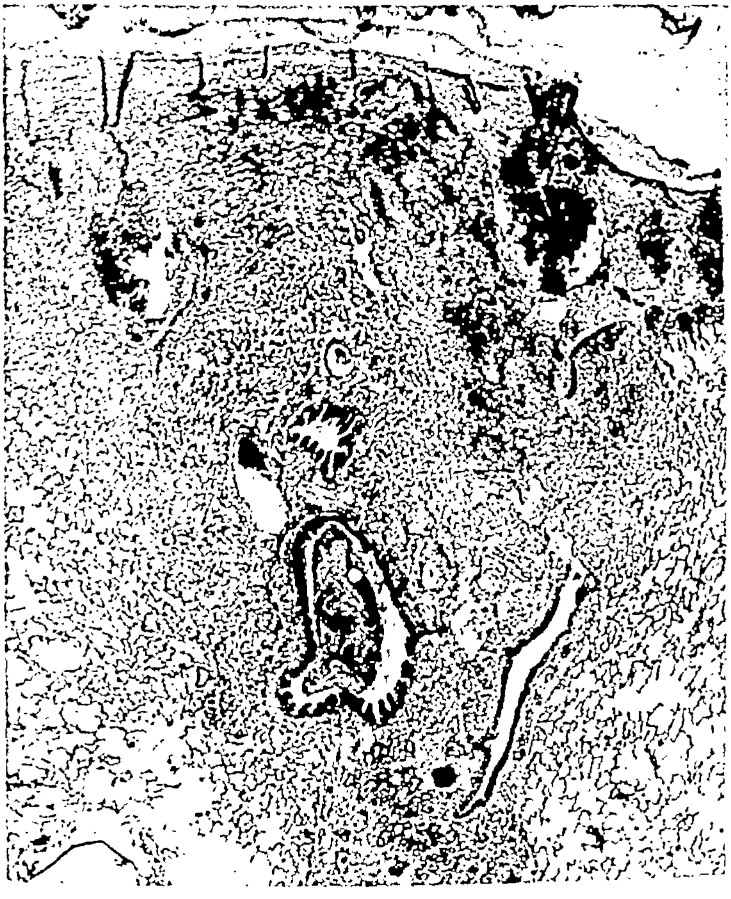

Fig. 9.—Defect following amputation of the tip of the right middle lobe six days after surgery. The bronchus was closed by a mattress suture. Note the parenchymal degeneration, distortion, and endobronchial exudate (X31).

The animal killed at two weeks was different from the rest because the branch of the pulmonary artery to the lower lobe was ligated. The pleura contained dilated blood and lymphatic vessels. There were scattered small scars throughout the lower lobe, and fibrosis in the wound was extensive. The wound contained several small abscesses.

The changes between the eleventh day and third week were minimal. At four weeks the scar of the segmental wound was mature, contracted, and thinner. There was slight parenchymal distortion due to contraction of the scar. Some endobronchial exudate in the wounded lobe was noted.

By the end of the sixth week, the wound was covered by a thin band of fibrous tissue that was undergoing hyalinization (Fig. 7). Many capillaries were present throughout the scar. In places it was covered by a single layer of cells that had many characteristics of adjacent pleural cells (Fig. 8). The interlobular septa were thickened by fibrous tissue which extended from the surface scar. A disturbing feature was the presence of plugs of exudate in some of the bronchi. Close to the bronchi were small abscesses and areas of pneumonia. It could not be ascertained whether this infection was incidental or secondary to the defect.

Following amputation of a portion of the middle lobe and closure of the open bronchus by suture, wound healing progressed in a characteristic manner. On the second postoperative day, the parenchyma was normal except for distortion near the bronchial suture. From this point, the alveolar walls radiated out in every direction. The alveoli were elongated and flattened near the suture. Between the wound and the suture, there was considerable hemorrhage into the parenchyma, deposits of fibrin, and invasion of all types of inflammatory cells, especially polymorphonuclear leucocytes. On the following day the capillaries near the wound were engorged and the inflammatory elements were greatly increased.

On the fifth day the middle lobe defect peripheral to the suture consisted of degenerating, airless parenchyma. There was active fibroplasia throughout the damaged area and this activity extended over the adjacent pleural surfaces. In the damaged area of the wound six days old, there were numerous clefts that represented intact alveoli caught in the organization (Fig. 9). Thereafter, organization of the wound and the adjacent distorted lung proceeded rapidly. By the eleventh day the surface of the lesion was invested by a dense fibrous layer. Fibrosis elsewhere was diffuse and less compact.

DISCUSSION

This study was designed primarily to determine the healing process of a lung wound following segmental resection in the cat. The portion removed was usually the apical segment of the right lower lobe. Although the chest wounds of these animals were closed without drainage, they had small postoperative pleural effusions. There was no demonstrable escape of air from the segmental wound. Because of residual pneumothoraces, few adhesions were noted during the days immediately after operation. After the sixth day, however, the wound usually was either adherent to the adjacent lobe or to the thoracotomy wound. The wound surface was invariably smooth despite microscopic evidence that the intersegmental plane was crossed occasionally at operation. Gross contraction of the wound was not observed until the ninth postoperative day. At no time was there gross distortion of the injured pulmonary lobes.

By microscopy, healing was ideal when only the anatomic segment was resected. Injury of the pulmonary artery or bronchus to the unpleuralized segment had a detrimental effect on wound healing and the adjacent parenchyma. There was evidence of local parenchymal ischemia and intra-alveolar hemorrhage where the intersegmental plane was crossed (Fig. 2). All of these digressions caused a significant inflammatory response.

Under ideal conditions healing progressed in the presence of few inflammatory cells. Polymorphonuclear leucocytes were virtually absent. The lesion was first covered by a film of blood clot which gradually became amorphous and thicker during the first postoperative week (Fig. 3). Fibroplasia was not active until the fifth day. At this time fibroblasts grew from the lung substance into the overlying film in a patchy manner. On the following day, the wounded lung was completely covered by these cells (Fig. 4). With contraction of the wound, there was apparent radiation of the alveoli from the surface of the lesion. New capillary formation in the wound covering was definitely evident on the eleventh day (Fig. 5). By the end of the fourth week, the scar was mature. From the third to the sixth week, it became progressively thinner. At six weeks, it was covered by a single layer of cells that were similar to the adjacent pleural cells (Figs. 7 and 8). The possibility that they were fibroblasts arising from the scar could not be excluded. Joannides and associates[6] thought that lung wounds ultimately were covered with endothelial cells.

When the dissection proceeded as planned, the border of the lung beneath the film was formed by alveolar walls (Figs. 1 to 3). During the first five postoperative days, the parenchyma subjacent to the wound was aerated but the alveolar caliber was often not as large as elsewhere (Figs. 1 and 2). This was partially due to widening of the septa. There were patchy areas of atelectasis in the injured lobes during the first five postoperative days. This pathology was seen in unoperated lobes only on the second day. Usually atelectasis was associated with collections of endobronchial exudate in the same sections. After the sixth day, this combination was not observed, and pulmonary aeration was complete. Pulmonary edema in the wounded lobes was present up to the fourth day when it was maximal. It gradually decreased thereafter.

Fibrosis of the lung was absent if there was no alveolar damage. With parenchymal injury, inflammatory changes ensued and fibrosis was eventually considerable. Microscopically, distortion of the lung was not an early manifestation. It occurred later with contraction of the wound and fibrous thickening of the interlobular septa (Fig. 6). Damage to the lung, however, was always followed by distortion of the alveolar pattern. The presence of endobronchial exudate four and six weeks after operation was disquieting. It was associated with peribronchial inflammation and small areas of pulmonary suppuration. From these limited observations it could not be determined whether this pathology resulted from diminished local resistance of the operated lobes.

The comparison of the segmental wound and middle lobe wound following
amputation of its tip is not entirely applicable since a bronchial sutu
in the latter. However, the combination of nonanatomic excision
caused a reaction far different than was seen after segment
was considerable strangulation and death of pulmonary
Inflammatory reaction was extensive and polymorphonu
numerous. Fibroplasia occurred earlier and it was mo
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Segmental resection was easier to perform in these animals than in human beings requiring the operation. This is understandable since a normal pulmonary segment in the human being is usually easier to excise than a pathologic segment. The lungs of the cats in this experiment were normal and the intersegmental divisions were found with facility. In spite of this, it was evident by microscopy that the intersegmental plane was crossed on several occasions. It may be assumed, therefore, that greater parenchymal damage of the remaining segment will occur during anatomic segmental resection for pulmonary disease. This is probably the cause of persistent alveolar and small bronchial leaks. If the removal of a diseased segment is difficult because of fibrosis at the intersegmental plane, the procedure probably should be changed to include an additional segment or to a total lobectomy.[7] On the other hand, when an anatomic segment can be removed with minimal parenchymal damage to the remaining segment, the lung wound will heal well without pleuralization. From the evidence presented here, approximation of the pleural edges by suture probably will cause unnecessary tissue destruction with subsequent local inflammation, fibrosis, and possibly infection.

CONCLUSIONS

In the experimental animal, a precise anatomic resection of a pulmonary lobar segment causes a wound in the lung that heals ideally. A mature surface scar develops over the course of four weeks with minimal distortion of the parenchyma. If lung tissue of the remaining segment is damaged during operative dissection or if sutures are taken, local fibrosis and distortion results. Occlusion of the bronchus or pulmonary artery to the wounded segment also alters healing. Following resection of an anatomic segment of a lobe, it is unnecessary and probably unwise to pleuralize the surface of the lung wound. It is suggested that segmental lobar resection in human beings be abandoned for an alternative procedure if the operator cannot dissect easily in the intersegmental plane. Many postoperative complications of segmental excision are related probably to undue trauma and residual disease at the line of resection.

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NOTICE

Applications for Membership

Applications for membership in the American Association for Thoracic Surgery must be sent to Dr. B. Noland Carter, Cincinnati General Hospital, Cincinnati, Ohio, before January 1, 1951.

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Original Communications

REPORT OF SERIES OF SINGLE-STAGE THORACOPLASTIES

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INTRODUCTION

IN THIS paper it is proposed that single-stage thoracoplasty is the operation of choice for many patients.

Originally it was intended to compare the results of single-stage and multiple-stage thoracoplastics. This comparison, however, was later considered impractical because indications for thoracoplasty five or six years ago were different from the ones that exist today and, since this series began five years ago, our own multiple-stage procedures could not be used as controls.

This series was begun cautiously because all generally accepted standards indicated that a single-stage procedure was hazardous. These standards developed out of the many disasters that occurred in the earlier period when thoracoplasty was an extensive, single-stage operation with the removal of many ribs. The pendulum swung from this extreme to the opposite, a patient having to undergo several major operations in which one, two, or three ribs were removed each time. We believed that with the improvement in anesthesia, surgical technique, and methods for the control of shock, more extensive resections could be undertaken.

The early cases consisted of patients with unstable minimal disease in whom we were unable to establish artificial pneumothorax. After periods of observation varying from four to eight months, it was decided to produce a selective collapse by thoracoplasty, which would approximate that resulting from an ideal selective pneumothorax.

Since the results with these early small thoracoplasties done in one stage were encouraging, it was decided to increase the number of ribs removed at one operation in selected cases with more extensive disease.

If this could be done safely there would be certain evident advantages. Instead of two or more operations, one would suffice. The interference with

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Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

collapse of the apex, due to resistance created by organizing tissues or early rib reformation often encountered at a second stage, would be avoided. In many cases this would result in adequate collapse being obtained, by removal of fewer ribs.

As our experience increased, the complication most frequently considered a definite contraindication to this type of procedure, namely parodoxical movement of the chest wall, failed to appear clinically to any significant degree. We found, in addition, that postoperative shock was considerably less than that which usually followed the second stage of a standard thoracoplasty.

In this series 55 per cent were cases in which no previous collapse therapy had been attempted.

Since these patients were carefully selected, they all had the prime requisite for successful surgery—good general condition.

Age is not particularly important, the patients in this group ranging from 16 to 65. The age distribution as shown by Table I is approximately the same as that for any comparable group.

TABLE I. AGE GROUPS

UNDER 20 YEARS	20 TO 30 YEARS	30 TO 40 YEARS	40 TO 50 YEARS	50 TO 60 YEARS
7 (16)	32	21	9	(57) 3(61) (63)

It is naturally preferable to deal with unilateral disease but, as our figures show, this type constituted only 40 per cent of the series. The location of the diseased area to be collapsed is important and should be confined to the upper pulmonary area. There is no difference of statistical significance between right and left lung. The patient should be kept under observation for a period of at least three and preferably six months and in bilateral disease correspondingly longer. Contralateral disease must be under control or at least stabilized. Before the advent of streptomycin, artificial pneumothorax was used when it could be successfully initiated, otherwise a moderately prolonged period of bed rest. However, streptomycin, which we have used extensively since 1947, and more recently PAS have greatly aided in the preparation of a patient for surgery.

TABLE II. DISEASE.

Unilateral	25	Bilateral	47
Operative side		minimal to moderately advanced	
Cavity	28 cases	Size	2 to 5 cm.

Streptomycin is not given to all surgical patients routinely. Its use is indicated in acute exudative lesions, bronchial disease, and where a moderately large cavity is to be collapsed, with the possibility of spread resulting from aspiration of infectious material. In the first two it is given four to six weeks preoperatively, in the latter one week preoperatively, and in all instances continued for at least one month postoperatively.

In cases where the disease extends into the lower half of the lung, we frequently use pneumoperitoneum in addition to autibiotic therapy. When two

TABLE III. PROCEDURE

	Left side	37	Right side	35
Ribs per stage	4	5	6	7
Number of cases	26	36	6	4

methods of therapy are used at the same time it is difficult to assess accurately their respective value. We do believe, however, that pneumoperitoneum is of some benefit in stabilizing mid-lung or lower lung disease.

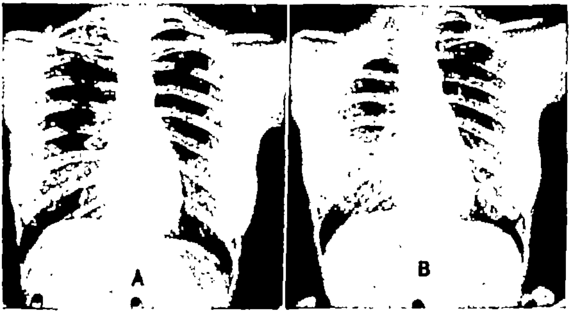

Fig. 1.—Four-rib thoracoplasty.

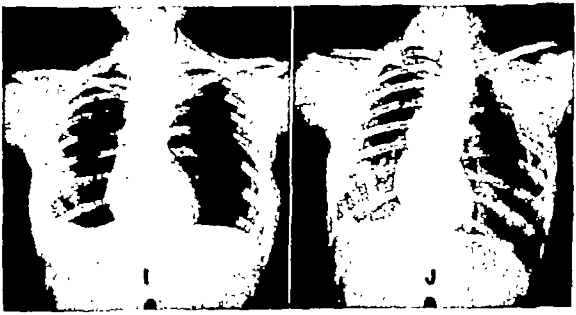

Fig. 2.—Five-rib thoracoplasty.

Investigation is begun with admission to hospital and a tentative opinion is given at that time as to the possibility of surgery for each patient. If it is considered a probability, any intervening treatment is undertaken with this in mind. Routine blood work, complete radiologic study including planograms, and bronchoscopy are done. All this work is repeated as indicated during the period of observation. We do not use the vital capacity test routinely nor have we the facilities for bronchospirometric estimation.

Surgeons who are on the resident staff of a sanatorium and who see patients day after day over a period of months or years, become quite adept in the clinical evaluation of the individual patient. During the period of personal observation, if a patient at any time shows enough signs of dyspnea to indicate the desirability of a vital capacity test, we consider that, in itself, a contraindication to the single-stage operation.

The operative procedure is done under endotracheal cyclopropane anesthesia, supplemented by small amounts of ether.

The incision parallels the medial border of the scapula, and extends from the base of the neck to the anterior axillary line. The muscles are sectioned and the serratus fibers severed from the second rib. The first rib is removed entirely up to, and often including, the costal cartilage. Depending on the extent of the disease, all or moderately large portions of the second and third ribs are resected. Portions of the remaining ribs, four, five, six, or seven, are removed in such a way as to provide gradual tapering of the thoracic cage. The transverse processes of all ribs involved are resected routinely except that of the first. The incision is closed in layers with the scapula outside the ribs when the number removed is not more than five. When the sixth rib is taken out the position of the scapula is ignored and it often falls of its own accord behind the ribs.

TABLE IV. SPUTUM CONVERSION

TIME	3 MONTHS	4 MONTHS	5 MONTHS	6 MONTHS	6 TO 12 MONTHS
	25	6	5	4	10
Preoperative sputum					
Positive		58			
Negative		14			
Conversion		50			
Persistent positive		8			
Source					
Operative side		5			
Bronchial disease		4			
Patent cavity		1			
Opposite side		3			
Persisting preoperative					

TABLE V. POSTOPERATIVE HOSPITALIZATION.

6 MONTHS	6 TO 12 MONTHS	12 TO 18 MONTHS	18 MONTHS	IN SANATORIUM
7	35 (Av. 9 mo.)	18 (Av. 15 mo.)	7	4
	Discharge 59%		9 months postoperatively	

TABLE VI.

	WORKING	WELL	MAXIMUM BENEFIT	IN SANATORIUM
3 to 5 years (13)	11	1 (retired man, 65 years old)	1 (asthmatic)	
2 years (35)	33	1 (retired man, 65 years old)		1 (disease, opposite lung)
1 year (24)	20			3 (1 bronchial, 1 bone, 1 revision)
	Recovery		67 or 94%	

All patients receive intravenous saline during the operation but routine transfusion of whole blood is given only when six or seven ribs are to be removed. This is due to our comparatively isolated location and our limited local supply of blood donors.

Postoperatively, dressings are applied tightly with adhesive. Sedatives are used as required. All patients spend a large part of the first forty-eight hours in an oxygen tent and appear quite comfortable within twelve hours.

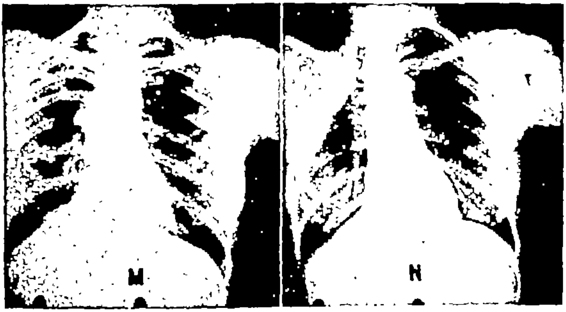

Fig. 3.—Six-rib thoracoplasty.

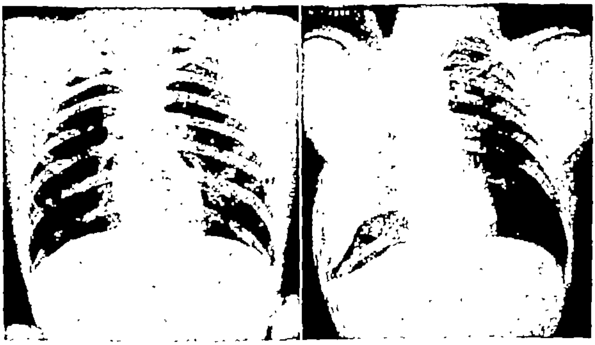

Fig. 4.—Seven-rib thoracoplasty.

In this series postoperative shock has been negligible and, as the operative technique is standard, we feel that some of the credit must go to our staff anesthetist.* Anesthesia is induced quickly with no distraction for the patient and continued at a light surgical level. The patient is usually awake within a few minutes following closure.

Other than the dressings applied at operation, which are taken off ten days postoperatively when the sutures are removed, we use no padding, harness, or other device to compress the collapsed area. The patient is constantly reminded to keep the head slanted to the operative side and to begin movement of the arm as soon as it can comfortably be done, which is usually in a few days.

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*Dr. Gordon Richardson, Muskoka Hospital, Gravenhurst, Ontario.

The results of this series we believe compare favorably with those obtained by multiple-stage procedures.

Table IV shows sputum conversion occurred in 25 cases within 3 months, 40 cases within 6 months, and 50 cases within 12 months. Of the remaining 8 cases, 4 became sputum negative on a second course of streptomycin therapy, and 1 required a revision with more extensive resection.

In considering postoperative hospitalization, it must be remembered that we are dealing with tuberculosis which is a chronic constitutional disease. Consequently the accompanying table of postoperative hospitalization showing the length of time a patient remains in residence after operation, is not of paramount significance in judging the success of the procedure. As it is, instead of speeding up discharge we usually have to use all our powers of persuasion to keep the patients in residence for a period which, in our opinion, is long enough to ensure continuance of recovery.

SUMMARY

We have presented a series of 72 cases of one-stage thoracoplasty with a minimum follow-up period of sixteen months. We would like to submit that this procedure is justified in a certain number of cases and find that with present extended and intensive antituberculosis campaigns, an ever-increasing number of cases fall into this select group. We have completed 21 one-stage procedures since this series. Of these 12 were six-rib and two seven-rib operations. We are very satisfied with the results.

CONCLUSIONS

1. Complete thoracoplasty in one stage is a safe procedure in properly selected cases.
2. The one-stage thoracoplasty often permits adequate collapse to be obtained by the removal of fewer ribs than would be necessary in multiple-stage operations.
3. One operation is preferable to two or three if the results are comparable.

DISCUSSION

DR. JOHN ALEXANDER, Ann Arbor.—Dr. Laird's and Dr. Lindenfield's proposal is interesting and challenging and their results are very good. As part of a critical analysis of their proposal, I am impressed by (1) the relatively inextensive lesions illustrated in a number of the preoperative roentgenograms shown in the lantern slides and (2) Dr. Laird's statement that a considerable percentage of the patients had had no previous collapse therapy; several temporary phrenic paralysis operations with or without a phrenic belt or pneumoperitoneum, or pneumothorax might have been expected to bring about a recovery of at least some of these patients.

I doubt if the demonstrated safety of a one-stage thoracoplasty for relatively inextensive lesions would be duplicated in cases in which the lesions are as extensive and severe as those for which thoracoplasty is so frequently used in many clinics. In the latter group, the cavities are often large, the sputum amount great, and the patients are frequently debilitated by prolonged tuberculosis. In such cases a one-stage thoracoplasty of six or seven ribs would, I believe, expose the patient to the real dangers of a sudden, great collapse of the extensive tuberculous lesions and to the exaggerated paradoxical respiratory movements that notoriously are likely to occur when even as few as four or five ribs have been widely resected in patients who have many pulmonary secretions to cough up and who may be dyspneic. When there is such paradoxical respirations, sputum is difficult to raise adequately and, under this circumstance, a spread of the tuberculosis in either or both lungs, or atelectasis, often occurs.

When the extensive one-stage Brauer-Friedrich thoracoplasty was used 43 years ago, the mortality was so high that it was soon abandoned. The pendulum then swung far in the opposite direction when Wilms and Sauerbruch resected only narrow paravertebral segments of approximately eight ribs; although this operation was usually performed in one stage, it was much safer than the Brauer-Friedrich operation, presumably because of the total length of the resected ribs was so much less. As the percentage of complete healing of the tuberculosis after the Wilms-Sauerbruch thoracoplasty was disappointingly low, the Brauer-Friedrich *type of operation, performed in multiple stages, was finally adopted as being both* effective and safe.

I believe that if an extensive one-stage thoracoplasty for extensive far-advanced tuberculosis should be used, the mortality rate would be high, and that the operation would then be rejected.

DR. FRANCIS M. WOODS, Brookline, Mass.—As Dr. O'Brien reminded us in his address, multiple-stage thoracoplasty when properly done is one of deserved reputation and a mainstay in surgical treatment of pulmonary tuberculosis. Physical setback, psychic trauma, and cost attending multiple stages have, nevertheless, been a source of disappointment. We would advise great caution in increasing the extent of single-stage operations unless some principle is used to overcome paradoxical movement of the decostalized chest wall. We have devised a two-stage procedure which applies this principle, and has been used since December, 1948, in 76 cases of cavitary disease, including many with extensive or bilateral cavitation, or both. Twenty patients were 50 years of age or older and, of these, 5 were 60 or over.

(Slide.) At the first stage the periosteum is stripped from all the ribs that would be removed in the usual multiple stages. We have stripped a mamixmum of nine ribs at one time and this was well tolerated.

(Slide.) The space between the ribs on the outside and the intercostal bundles and periosteal beds on the inside is filled with Lucite balls, thus immobilizing the chest wall. In addition, a good layer of tissue with abundant blood supply is interposed between the lung and plombage. The incision is closed.

After four weeks there is adequate fibrosis and rib regeneration in the chest wall to prevent paradox. The second stage is done, removing the Lucite balls and the deperiostealized ribs, including the transverse processes and the first rib.

The sputum has been converted in 16 out of 20 patients, on whom operation was completed more than six months previously. There have been no infections. The danger of late infection or erosion is eliminated by the second stage. The collapse obtained at a single sitting is better. Dr. Overholt and Dr. Kenny of our group are attempting to perfect a procedure which will do away with the second stage by fixing the deperiostealized ribs in an inverted position to stabilize the chest wall.

DR. F. B. BERRY, New York.—I have three slides which I wish to show merely from an historical standpoint, because when I first became a member of this Association and before, many at that period were doing thoracoplasty in a single stage and took out nine, ten, or eleven ribs at one time; roughly, as I recall, the results were looked upon as about in three equal parts—33 per cent died, 33 per cent had pretty good results, and 33 per cent went along with their disease uninfluenced or made worse.

These three slides show a thoracoplasty as it was done at that time and one of this patient taken a month ago. The operation was done when she was 14 years old. It is not the type of thoracoplasty we do today. She was one of the 33 per cent good results and she has earned her living ever since. She has no deformity and is now going along happily, and I thought that particularly some of the younger members, who were perhaps not even thinking of medical school when this patient was operated upon, might like to see them.

(Slide.) This is the original condition of this girl, with an extensive infiltrating lesion throughout the right side for which she was given pneumothorax.

(Slide.) Then she had the pneumothorax with a long stringlike adhesion. This was before the days of internal pneumonolysis, so no attempt was made to sever that. She also developed fluid, and Dr. J. A. Miller and Dr. A. V. S. Lambert believed that the next step should be thoracoplasty, and certainly from the standpoint of function and longevity they were right.

DR. CHARLES P. BAILEY, Jenkintown, Pa.—I did not intend to discuss this paper but feel that in justification to Dr. Laird and Dr. Lindenfield we must report that we, too, were rash enough to do a few large thoracoplasties in one stage. We have operated upon 15 or 20 patients recently, doing six or eight ribs at a time. We took off the transverse processes and the upper three or four cartilages. We were impressed by the fact that these patients did not have very much surgical shock, nor great paradoxical breathing. It does seem that things are quite different from a few years ago before we had the antibiotics, when resection of only three or four ribs sometimes gave us many anxious hours. We believe that probably the greatest factor in this changed situation is the better management of secretions, and perhaps pretty good selection of cases. We do not do any borderline cases by the one-stage thoracoplasty.

We have found that if we attended to secretions the patients did not have much trouble with paradoxical breathing. If there was any evidence of excessive bronchial secretions, we bronchoscoped them immediately. And if that seemed to be required repeatedly, we did not hesitate to perform a tracheotomy, and did so in four cases. There was no mortality in this series, and in each instance the collapse was perhaps somewhat superior to that obtained in the usual staged procedures.

DR. LAIRD (closing).—Dr. O'Brien warned me that the roof would fall on us; fortunately we are still here. I quite agree with Dr. Alexander, naturally, that these patients are not the extensive and sick patients that are possibly most suitable for thoracoplasty. This is a select group; many of them have had pneumothorax attempted; many are primary thoracoplasties. I think the swing has been toward more frequent thoracoplasties in recent years of a primary nature—that is, for localized lesions, localized apical lesions, in an otherwise well-controlled individual. I believe that in that type of patient, this operation of one-stage thoracoplasty is safe; we have had no mortality in this group. It accelerates the patient's recovery and I think, keeping in mind these factors and the selection of cases, that it is a safe procedure.

FURTHER EXPERIENCES WITH SEGMENTAL RESECTION IN TUBERCULOSIS

J. MAXWELL CHAMBERLAIN, M.D.,* AND (BY INVITATION)
ROBERT KLOPSTOCK, M.D.,† NEW YORK, N. Y.

INTRODUCTION

SEGMENTAL resection of the lung is comparatively new in the surgical treatment of tuberculosis. Its objective is to remove not only the diseased components but to preserve the maximum amount of normal lung as well. Though the procedure was done with some hesitancy at first,[1, 2] nevertheless we wish to present our experiences with the first seventy-five consecutive cases done in the last two and one-half years. We are anxious to draw no conclusions at this time because the number of cases is too small and the follow-up period is too short for definitive evaluation. Suffice it to say that the results have been such that we are encouraged to continue its use in carefully selected cases.

GENERAL CONSIDERATIONS

Resistance, both systemic and local tissue immunity, is just as important to the success of segmental resection as in all other forms of therapy in tuberculosis. Resistance, we all know, often compensates for the limitations of surgical therapy, but a major surgical operation rarely alters the course of a tuberculous patient who has little or no resistance. Proper timing of the operative procedure in tuberculosis has been repeatedly emphasized by John Alexander and other early workers in this field. This was another way of warning the surgeon not to operate upon a patient who lacked resistance, and our best results in segmental resection have been in patients who had this important factor.

Resistance is a difficult entity to define, but its existence usually is based upon the composite picture. The *age, race,* and *family history* formulate the patient's background; the *present illness* reveals the degree and duration of *toxicity* up to the time of surgical consideration. The changes in the *physical findings* (observation, palpation, percussion, auscultation), the *vital signs* (temperature, pulse, and respirations), *laboratory studies* (sedimentation rate, red blood count, hemoglobin, etc.), *sputum changes* (character, amount, bacterial content), the *x-ray evidence* (calcification, elevation of interlobar fissures and hilum, mediastinal shift, intercostal narrowing, scoliosis, elevation of diaphragm, resolution, and localization), and finally the very important but intangible factor, *general condition* (appearance, appetite, weight, etc.), when all added together, accurately evaluated and properly weighed leads one to the conclusion that the patient either does or does not have resistance. *To the patient with resistance, surgery is a great adjunct.*

Work done at Triboro Hospital, St. Albans Naval Hospital, Halloran Veterans Administration Hospital and Bellevue Hospital.

Read before the Thirtieth Annual Meeting of The American Association for Thoracic Surgery, Denver, Colo., April 15-18, 1950.

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culosis, however, have little regard for these indefinable borderlines, and often at operation the residual evidence of the previous inflammatory reaction can be recognized in the form of "fibrous scarring" as the intersegmental plane is developed. When this reaction is severe and progress along the normal anatomic border too closely approaches the active disease, an adjacent subsegmental bronchus may be palpated, isolated, divided, and the subsegment removed with the total specimen.

The vascular pattern as pointed out by Boyden and Scannel is characterized by its inconsistency, but the bronchial tree is more reliable. Therefore, the proper bronchus should be identified and divided first. The bronchus can be identified first in both superior segments of the lower lobes and the posterior and apical segments of the right upper lobe, but on the left the apical-posterior bronchus is concealed usually by one or two arteries. No arteries concealing the apical-posterior bronchus, however, should be ligated until *all* branches to the left upper lobe have been identified. The origin of the artery to the left anterior segment has come off the parent artery to the apical segment on occasions, and in two instances it has come off just proximal to the lingular artery. The latter, on the other hand, may originate as one or two vessels, or may come off of the anterior segmental artery in front of the bronchus. These experiences and the teachings of Boyden and Scannel have made us very cautious about ligation of any vessel on the left until all are visualized. Traction upon the distal bronchus soon discloses the associated artery which is isolated, ligated, and also divided. Gentle traction then on these two structures permits the surgeon to begin the segmental resection.

The veins, however, deserve separate consideration. They lie in the intersegmental plane and receive tributaries from the segment to be removed as well as the segment to be left behind. The small tributaries from the segment being removed are often torn across at their junction with the intersegmental vein before they are actually identified. Others are large enough to be ligated and divided, but it is a good general rule to delay the division of any vein until absolutely necessary. In some cases the previous inflammatory reaction has so altered the anatomy that it is extremely difficult to preserve the intersegmental vein. However, other collateral channels are available for venous return if the intersegmental vein is damaged or ligated. Usually, the intersegmental vein can be preserved.

COMPLICATIONS

The number of complications have decreased as our experience increased. The last forty-one consecutive cases have been done without a major complication or death. We previously made the statement that the morbidity in segmental resection was greater than after lobectomy. Our experience now with more than 250 segmental resections for all types of pulmonary disease allows us to believe that not only the morbidity but the mortality rate (2.4 per cent) is no greater than after lobectomy.

MINOR COMPLICATIONS

The absence of operative spreads was a surprise finding. The two spreads which occurred later were associated with the development of a bronchopleural fistula. Local exacerbations in the intersegmental plane were not detectable, if present.

One small superficial wound infection had been incised unsuccessfully on two occasions. The patient's sputum was repeatedly negative on culture.

There were two failures of the lung completely to reexpand and obliterate the pleural cavity. One of them (W. T.) was in a patient who also had a decortication of the entire lung at the time of segmental resection. In both patients the spaces were obliterated by removing short posterior segments of ribs 4, 3, and 2. The resection in each case had been done through the 5th rib bed.

MAJOR COMPLICATIONS

There were six patients who developed a bronchopleural fistula and were automatically classified as empyemas and reexpansion failures. In only two of these was there evidence of extension. Now one is culture negative after additional surgery, three are persistent (one of these is negative), and two died.

One patient (L. S.) had the left apical-posterior segment removed, developed a bronchopleural fistula which failed to close by a myoplasty and thoarcoplasty. A pneumonectomy was then done. The patient is now well and the sputum is culture negative.

Another patient (G. H.) had the same postoperative misfortune and now has a small bronchopleural fistula after the pneumonectomy. Her sputum is culture negative. She is still very ill, however.

Another patient (J. B.) who had bilateral small cavities developed a bronchopleural fistula after removal of the left apical-posterior segment and has had three attempts at closure by myoplasty and thoracoplasty. We now believe the positive sputum from the opposite chest infects our grafts and working environment which slowly breaks down after each surgical attempt at closure. The next surgical attempt will be directed at the source of the positive sputum in the opposite lung.

Another patient (G. P.) had a contralateral pneumothorax, and it was planned to do an *apicosposterior* segmental resection if technically possible. Laminographs, however, suggested considerable disease in the anterior segment of the left upper lobe. A preliminary small thoracoplasty was done in view of the possibility of a lobectomy. At operation the decision was changed from a segmental resection to left upper lobectomy. The fissure was obliterated between the apex of the lower lobe and upper lobe because of disease on both sides of it; therefore, the superior segment of the lower lobe was taken rather than divide the fissure. The superior segment in this case was a very large one, and the three remaining basilar segments were entirely too small to fill a reduced but relatively large pleural space. The upper two-thirds became opaque after operation, the tubes plugged, and it was felt that a serosanguineous coagulum had developed which filled the upper chest. On the seventh postoperative day, streptokinase was introduced into the region of the coagulum, and one hour later the patient opened a bronchopleural fistula and spat up about 600 c.c. of serosanguineous material. During the year that followed he developed fluid on the side of the pneumothorax, this became turbid and positive for acid-fast bacilli. Later he developed a homologous serum hepatitis from repeated blood transfusions, re-expanded his contralateral lung, and though his general condition is poor at the present time he is gaining weight at the rate of one pound a week. His sputum is positive and his fistula still open.

Two other patients died, and are reported below.

EXACERBATIONS

Late exacerbations have occurred in five instances. In one instance (A. E.) several months after discharge a small shadow appeared in a follow-up x-ray on a patient whose sputum had been repeatedly negative to culture examinations. The patient was asymptomatic but had one positive sputum culture. The shadow disappeared one month later after administration of streptomycin at home. Sputum cultures are now negative.

Another patient (G. A.) subsequent to discharge developed an intermittently positive sputum culture. Hospitalization, bronchoscopy, x-rays, and laminographs have failed to disclose the source of the positive culture. He is intermittently positive on gastric lavage. This patient has had no prolonged postoperative streptomycin, and probably has a bronchial ulcer beyond the vision of the bronchoscopist.

Another patient (M. D.) with lymphohematogenous tuberculosis and a positive urine had a right upper lobectomy and segmental resection of the superior segment of the right lower lobe. Six months after several negative sputum cultures she reactivated an old lesion in the right lower lobe and became positive. A temporary phrenic crush and pneumoperitoneum failed to change the residual shadow in the right lower lobe. Resection of the right middle lobe and basilar segments of the right lower lobe has converted her sputum cultures.

Two other patients (E. G. and R. F.) have late exacerbations and have not yet cleared on conserative therapy. Neither had streptomycin before, during or after operation.

FATALITIES

One fatality occurred in the first 25 cases. The patient was a 57-year-old man. The operation was easily accomplished, and the patient was considered in good condition twenty-four hours after operation. He requested a glass of water and, a few minutes later upon the nurse's return, respirations had ceased and he was pulseless. Autopsy revealed a collapsed lung on the side of the operation, but the intrapleural tubes had not been clamped post mortem; and breath sounds were heard just prior to death. The patient's family then reported he had had two "heart attacks" prior to the hospitalization which he had not disclosed fearing that the operation would be denied him. A preoperative electrocardiogram was essentially normal.

A second fatality occurred in a healthy 30-year-old man. During the resection of the right apical and posterior segments, the cavity was entered by accident. The intersegmental plane had been destroyed by the inflammatory reaction. In retrospect a lobectomy should have been done. A bronchopleural fistula developed, the lung failed to expand and obliterate the dead space, an empyema occurred, and the patient spread to the lower lobe on the side of the operation. Approximately nine months later a pneumonectomy was done as a desperate gesture to avoid an anticipated fatality. At the end of the operation an anesthetic accident accounted for the patient's death. The outcome might have been the same had the accident not happened.

The third fatality occurred in a 40-year-old patient who had had a *right* 7-rib thoracoplasty subsequent to which he had a bilateral extensive spread. The lungs cleared except for a cavity in the apical-posterior segment of the *left* upper lobe. Function was greatly reduced, and therefore a left extrapleural pneumothorax was done because it could be done under local anesthesia and is a reversible procedure in the first few days. He stood the operation fairly well, and six weeks later a thoracoplasty was laid down to maintain the collapse obtained by the extrapleural pneumothorax. The sputum remained positive, and tomographs disclosed a cavity beneath the thoracoplasty. Functional studies (broncho-spirometry) at this time were borderline. A segmental resection of the apical-posterior segment was done beneath the thoracoplasty. The patient developed a bronchopleural fistula and a small empyema which was drained. He lost ground, gradually became more and more debilitated, and died ten months after operation. The sputum was negative, and autopsy revealed no active disease. Cause of death was respiratory insufficiency. No active disease was present in the specimen and patient's sputum was culture negative at the time of death.

DISCUSSION

INDICATIONS

The indication for this procedure may be inferred from the term segmental resection. In other words, when the main offending focus is well localized to one or two segments, consideration should be given to this procedure. The final decision, however, depends upon many of the same prerequisites used in selecting a patient for lobectomy. Though some of our patients would have been poor candidates for a successful thoracoplasty, many of them would have had a thoracoplasty and probably a successful one in other surgical environments. We must admit, but with some hesitancy, that in localized lesions we are using segmental resection not only instead of, but in preference to a thoracoplasty. Some, of course, are done in conjunction with a thoracoplasty, but the dimensions of the two procedures are much smaller than when only a thoracoplasty is done to control the focus.

The operation is a meticulous one and the statement above must be modified. The morbidity and mortality rates after a thoracoplasty are low in the year 1950. This was not true twenty-five years ago. The morbidity and mortality rates of segmental resection are greatest now. As our experience increased they became increasingly low. The morbidity and mortality rates in the last forty-one consecutive cases have been comparable in every way to the thoracoplasty figures. Our anxiety now is directed toward the late follow-up results.

In retrospect, our mistakes are obvious and many can be avoided in the future. In the beginning we were cautious in our case selection, and there were few complications in the first twenty-five cases. Then we grew bolder and accepted a few hazardous risks. Our complications and deaths occurred during this period. Upon returning to the well-localized lesion in the patient with resistance our major complications have disappeared for the moment, at least. To establish segmental resection as a reasonable and secure solution in selected cases we wish to emphasize the following principles in management.

LAMINOGRAPHY

Laminography, especially the lateral "cuts," as recommended by Klopstock[14, 15] are essential to accurate evaluation of the disease and its location. Undoubtedly, those who were first engaged in resection therapy made many mistakes because neither laminography nor steroscopic films were used in case selection. Laminography has given us few, if any, false leads. In fact, by crosschecking the surgical specimen with the laminograms our confidence in such studies has increased. Also at the time of segmental resection the palpation of small indolent or active foci is less accurate than serial x-rays and laminographs in determining the activity of a lesion or given focus. On occasions at operation we have changed our decision from segmental resection to lobectomy because of small palpable foci in the anterior segments, only to have the pathologist inform us that the lesions in the questionable segment were firmly and securely healed. At present we are remaining faithful to the preoperative recommendation whenever it is technically possible.

Furthermore, the lateral "cuts" usually outline the fissures and the compensatory spacefilling aspects of the residual segments may be estimated. For example, the position and size of the anterior segment on the right is known as soon as the middle lobe fissures are located; or the size of the apical and posterior segments may be estimated upon identification of the fissure between the superior segment of the lower lobe and the upper lobe. In this series only three patients have not had laminographic studies.

STREPTOMYCIN

Streptomycin was used in 80 per cent of the cases. In selected cases with well localized lesions and little or no sputum streptomycin was not used. The use of streptomycin is designed to accelerate the localization and maturity of a lesion. Its administration before operation must be individualized. Some patients may be prepared in one week, others in three or four weeks. Its use after operation is also variable. In general it should be continued for six weeks to three months after operation. Based upon the work of Meisner, Wilson, and Overholt who demonstrated microscopic intramural tubercles at the point of bronchial division, it might be used routinely to secure firm healing of the bronchus. Also at the time of segmental resection small indolent or active residual foci may be left behind.

REEXPANSION

Obliteration of the dead space after operation is considered an important principle in the prevention of a tuberculous empyema. Physicians years ago were aware of this principle in the management of a pneumothorax. When an empyema was imminent the lung was quickly reexpanded to avoid maturity of the empyema. It must be assumed that the pleural space is always contaminated during resection therapy, but still the development of an empyema is rare after a segmental resection if this principle is respected.

The dead space cannot be obliterated early after a pneumonectomy, but the pleural cavity, like the peritoneal cavity, can defend itself against a mild infection provided the source of infection is removed or abated. At Sea View Hospital a cavity perforated into the pleural space ten days after a closed intrapleural pneumolysis. The surgical staff of this hospital treated the patient as though an appendix had ruptured. The lobe was resected, and the pleural cavity obliterated immediately by reexpansion of the other two lobes. An empyema did not develop. Though streptomycin was also used, the same result might have been achieved without it. Overholt, for example, before streptomycin was available, has opened cavities and packed them with gauze before proceeding with the operation. He used this technique in large cavities with large amounts of sputum to prevent "spreads." We have accidently broken into cavities during a lobectomy on patients who were either streptomycin fast or were not given it prior to operation, but, if the dead space was obliterated, an empyema did not develop.

The dead space in segmental resection is easily obliterated usually. This is not true, however, if a lobectomy and superior segment is to be removed. In such cases a preliminary "tailoring" of the thorax seems indicated and should be designed to fit the residual healthy components. Obliteration of the dead space after segmental resection is easiest in the first seventy-two hours. Daily x-rays and close attention to the mechanics of the intrapleural suction tubes during this period are paramount.

LOWER LOBE DISEASE

Segmental resection finds its greatest usefulness when the disease is localized to the superior segment of the lower lobe. Disease in this location has been difficult to treat and, though pneumothorax, pneumoperitoneum, cavernostomy, and temporary paralysis of the diaphragm have been successful on occasions, in our experience these procedures have *not* been *consistently* reliable. Until segmental resection was tried it was our custom to do either an extensive thoracoplasty or lobectomy, but always with a feeling of dissatisfaction because of the physiologic sacrifice.

FUNCTIONAL ASPECTS

The functional gain by leaving in the anterior segment of the upper lobe is not in itself significant. Its presence as a "filler," however, is thought to be extremely valuable to the function of the other pulmonary components. In segmental resection the degree of pulmonary distention is reduced and there is much less anatomic distortion of the tracheobronchial tree.

The residual lobes after an upper lobectomy are vulnerable to infection, both tuberculous and nontuberculous, because of (1) the angulation of the tracheobronchial tree, and (2) the degree of overdistention. The elongation and foreshortening of the bronchial tree with each respiratory effort, twenty-four hours a day, supported by ciliary action and cough, accounts for our bronchial hygiene. Segmental resection disturbs this balance least.

In some cases of pneumothorax therapy the role of bronchial peristalsis is best appreciated. The bronchus to the immobile lung which has been "trapped" is "dirty" by comparison with the moving opposite lung. The mucosa is often covered by a thin white or grayish precipitate which wipes off and leaves a red congested mucosa beneath. This was noticed in the "trapped" lung in nontuberculous war injuries as well. Upon reexpansion, however, normal hygiene is restored. Bronchial peristalsis is on duty continuously, and its protective importance cannot be overemphasized. The emphysematous lung with the patient in a prolonged inspiratory state cannot foreshorten the chronically elongated bronchial tree, and almost all emphysematous patients experience, therefore, frequent episodes of pulmonary suppuration, and have variable amounts of bronchiectasis.

SUMMARY

Segmental resection in pulmonary tuberculosis is designed to remove the major pathologic focus with little physiologic sacrifice. Resistance and localization are essential to the desired result. Streptomycin not only accelerates maturity of the lesion, but may aid in bronchial healing.

Cavitary pulmonary tuberculosis in man is a disease confined usually to the apical and posterior segments of the upper lobes and the superior segments of the lower lobes. Laminography, especially the lateral "cuts," is paramount to accurate localization of the lesion. As the lesions heal and contract, slow compensatory distention occurs in the normal lung components. After segmental removal the additional distention is slight and of little significance.

The operation is a meticulous one, requires close vigilance in the early postoperative period, and if the dead space is obliterated by early reexpansion of the lung, complications rarely occur. For this reason when a lobectomy and segmental resection are contemplated, one of five methods should be used to assure obliteration of the dead space.

Three patients died, but the operation as such was responsible for only one. In the seventy-five cases, sixty-five (86.7 per cent) were culture negative, but the follow-up period was short. Only two spreads occurred in the entire series.

but six developed bronchopleural fistulae. Two of the latter are dead, two required additional surgery for closure, and two persist. Five [illegible] have occurred—they are not extensive.

In the last 41 consecutive cases no major complication has occurred. Segmental resection has several advantages over a thoracoplasty for the same type of lesion, and we believe that careful selection and increasing experience may prove it to be the superior procedure.

(See discussion on page [illegible].)

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RESECTION IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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INCREASING indications for resection in the treatment of pulmonary tuberculosis emphasizes the need for careful appraisal of its effectiveness in controlling the disease and of the hazards incident to its use. With better surgical and anesthetic techniques the trend is toward lower morbidity and mortality rates but even with streptomycin protection they are still much too high. A recent report by Sweet[1] concerning the late results of resection in 63 patients treated in the pre-streptomycin era presents an especially pessimistic view of the range of usefulness of resection. Of 27 patients who had lobectomy, 9, or 33 per cent, are dead; 6, or 22.2 per cent, are alive with evidence of active disease; and 12, or 44.4 per cent, are apparently well. In the pneumonectomy group of 36 patients, 19, or 52.8 per cent, are dead; 3, or 8.3 per cent, are alive with active disease; and 14, or 38.9 per cent, are apparently well.

In 1947, Overholt and associates[2] reported a series that is representative of the early streptomycin era. Of 35 lobectomies, 11 per cent are dead, 57 per cent are clinically well with negative sputum, and 20 per cent were too recently done to classify. Thirty-three, or 48 per cent, of 69 pneumonectomies were living and well with negative sputum; 17 per cent were dead and 16 per cent were too recent to classify. They also point out the greatly decreased incidence of spread of disease and bronchopleural fistula. Although this lower incidence of complications must be largely attributable to streptomycin protection, the advantage of the face-down position is thought to be a factor of considerable importance.

Bailey and co-workers[3] in 1949, reported a comparison of results in 100 resections without streptomycin and 100 resections with streptomycin. A marked reduction of contralateral tuberculous spread and tuberculous empyema was noted in the streptomycin treated patients. They also observed a marked reduction in mortality in the patients with acute pneumonic disease and extensive lung destruction in the streptomycin group.

The results of the tuberculous resections done at the Mayo Clinic were reported in 1948 by Clagett and Seybold.[4] There were 2 early deaths and 1 late death in 15 pneumonectomies and 1 late death in 14 lobectomies. Five had active disease and 1 was untraced at the time of the report. Early spread occurred in 2 pneumonectomies (13.3 per cent). Late spread occurred in 4 lobectomies (28.6 per cent) and 2 pneumonectomies (13.3 per cent). Two pneumonectomies developed bronchopleural fistula. Tuberculous empyema occurred in 1 lobectomy and in 1 pneumonectomy. One pneumonectomy was complicated by a nontuberculous empyema.

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Gale, Dickie, and Curreri[5] recently reported the results of 80 resections with an operative mortality of only 2.5 per cent and a total fatality rate of 6.25 per cent, 83.75 per cent were negative and clinically well for varying periods up to three years following operation. Ipsilateral reactivation or spread occurred in only 2 instances and contralateral spread in six. There were no bronchopleural fistulas in 47 pneumonectomies and only 2 in 33 lobectomies, 1 of which was classified as temporary, the other causing death. The chief indications in this series were thoracoplasty failure, 51.25 per cent, and bronchostenosis, 26 per cent. Of the 31 thoracoplasty failures, 26 had pneumonectomy and 15 had lobectomy.

CLINICAL MATERIAL

This report deals with the results of resections for pulmonary tuberculosis performed in our clinic from 1945 to Nov. 1, 1949. Prior to 1945, only occasional resections were done for pulmonary tuberculosis and with few exceptions were done by means of the tourniquet technique. Consequently, they have little statistical significance and are not included in this report.

TABLE I. RESECTION FOR PULMONARY TUBERCULOSIS

202 OPERATIONS	
Lobectomy	98
Pneumonectomy	104
Total	202

TABLE II. TYPE OF OPERATION BY SIDE

Lobectomy		
Right	65	
Left	33	
		[illegible]
Pneumonectomy		
Right	55	
Left	49	
		[illegible]
Total		[illegible]

There were 202 operations performed u
which were lobectomies and 104 of which were
were done on the right side in 65 instances and o
were 55 right pneumonectomies and 49 left pne

Only 9 segmental resections were done in the
they were not deliberately planned but were
avoid pneumonectomy when disease occurred
which the lesion was originally localized. In
tions lobectomy was done in an effort to
though the lobe or lobes allowed to remain
palpable disease.

One hundred and nineteen of the
There were 36 (18 per cent) Negroes,
one American Indian. Mention is
racial groups because of their know

The youngest patient was 6 years of age and the oldest 73. Twenty-two were 50 years of age or over and 2 were in the seventh decade of life.

There was clinically significant contralateral disease in 87, or 43 per cent, of the patients. In 60 it was considered minimal or moderate in extent and in 27 it was extensive. In the latter group 4 had cavity and 10 had re-expanded pneumothoraces.

Since streptomycin became available it has been used for preparation of patients for surgery and for protection during the postoperative phase. It has been a useful adjunct to operation but, as is well known, its use is not always attended by success and certainly its misuse is occasionally attended by disaster.

INDICATIONS FOR RESECTION

The selection of lesions suitable for resection has been fairly well standardized as regards certain major classifications. Such obvious indications as failure of thoracoplasty, the presence of high-grade bronchostenosis and associated bronchiectasis are widely accepted. In this series there were 71 thoracoplasty failures (35 per cent), 33 with bronchostenosis (16.3 per cent), and 14 (7 per cent) in whom the primary indication was tuberculous bronchiectasis. The true incidence of bronchostenosis is not indicated in Table III because of the inclusion of at least 8 additional instances under the thoracoplasty failures.

TABLE III. INDICATIONS FOR RESECTION

Thoracoplasty failure	71
Bronchostenosis	33
Tuberculoma	26
Lower lobe disease	22
Tuberculous bronchiectasis	14
Disease not suitable for thoracoplasty	9
Destroyed lung	4
Post lobectomy fistula and empyema	1
Other indications	22
Total	202

Tuberculoma as an indication must be considered slightly controversial largely because of definition. There were 26 in this classification, or 12.8 per cent. These are represented mainly by the solitary round or conglomerate lesions with or without evidence of cavity, and by the so-called "filled" cavity. They are considered to be encapsulated caseous lesions with or without central liquefaction and/or bronchial communication. Also included in this group are a few instances of multiple encapsulated caseous foci limited to a lobe. Four additional cases originally thought to be tumor bring the total in this group to 30 or almost 15 per cent of all resections.

TABLE IV. OTHER INDICATIONS

LESIONS RESECTED—LATER PROVED TUBERCULOUS	
Peripheral round lesion	4
Atelectasis with negative sputum	10
Abscess or suppurative pneumonitis	4
Bronchiectasis	4
Total	22

Lower lobe disease, long recognized as frequently uncontrollable by the usual collapse measures, is a logical extension of the indications for resection. In this category, without any effort to further classify type of disease, are included 22, or 10.9 per cent. In this group is to be found the ubiquitous and troublesome superior division lesion of the lower lobe

Perhaps the most controversial of the indications is the upper lobe lesion for which thoracoplasty is ordinarily considered the procedure of choice. We believe that lobectomy should not be substituted for thoracoplasty where there appears to be reasonable chance for success with thoracoplasty and when there is not an obvious contraindication to thoracoplasty. We have selected 9 instances, 4.5 per cent, in which either the disease or patient were considered not suitable for thoracoplasty.

A few of these are children with progressive upper lobe disease, one an adult with pectus excavatum, and the remaining are tension cavities, or other lesions in which thoracoplasty failure seemed inevitable.

Destroyed lung is seldom considered an indication for primary resection except when due to high-grade stenosis. Thoracoplasty is thought to be the procedure of choice and is followed by resection in the event of thoracoplasty failure.

There was one patient who had had a lobectomy followed by fistula, empyema, and persistently positive sputum in whom pneumonectomy was completed.

TABLE V. COMPLICATIONS

202 RESECTIONS FOR PULMONARY TUBERCULOSIS	
Pleural	
Fistula and empyema	27
Hematoma*	5
Pericardial	
Effusion	2
Constrictive pericarditis	1
Adhesive pericarditis	1

*Two required secondary operation and evacuation of clot.

The other indications as noted in Table IV represent lesions which were thought to be tumor or suppurative disease prior to operation but in which the true nature of the disease was established by the microscopic sections. There were 22, or 11 per cent, in which the preoperative diagnosis was incorrect.

TECHNIQUE OF OPERATION

The Overholt face-down position is used routinely except for the occasional patient with a tuberculoma or other lesion from which minimal drainage of secretions is anticipated.

During the past one and one-half years anesthesia has been induced with pentothal and curare and maintained with intravenous procaine and endotracheal nitrous oxide and oxygen. Prior to the institution of this practice, the anesthetic agent used was endotracheally administered ether vapor and oxygen.

The pleural cavity is entered through the periosteal bed of the appropriate rib. The lobe or lung is mobilized by separation from the parietes with sharp dissection care being taken to avoid entering subpleural cavities or caseous foci of disease. The structures at the hilum are dissected individually, the vascular elements are ligated with silk, the bronchus is amputated, and the stump closed with end sutures of fine silk. The stump is covered with parietal pleura or other contiguous tissue whenever possible.

All lobectomies have one or more thoracotomy tubes placed in the pleural cavity and attached to water-seal drainage bottles until expansion is effected. The pneumonectomies are not drained. Pressures in the pleural space are maintained at optimum levels and streptomycin and penicillin are introduced by frequent insertion of the aspirating needle. Careful attention to blood replacement and fluid requirements is of course extremely important. Early ambulation and the maintenance of strict vigilance as regards the evacuation of tracheal secretions contribute importantly to an uncomplicated postoperative course.

COMPLICATIONS

The development of bronchopleural fistula and empyema was by far the most important and disastrous complication. Since empyema associated with fistula in the tuberculous are nearly always secondarily infected tuberculous empyemas, no effort was made to distinguish between tuberculous and nontuberculous empyema. In all except one instance, a fistula could be demonstrated in the empyemas complicating resection in this series.

This very serious complication occurred in 27, or 13 per cent, of the patients and was a major cause of death. In 5 patients resection was undertaken under conditions that were favorable for the development of fistula and empyema. In 3 of these empyema was already present and in 2 there were persistent bronchocutaneous sinuses following cavernostomy.

Pleural hematoma occured in 5 patients. Secondary thoracotomy was necessary for the evacuation of clot in 2 of these. Absorption of the hematoma occurred in the others.

Pericardial effusion was a late complication which contributed to death in 1 patient with disseminated tuberculosis and empyema. Another patient with pericardial effusion and ascites is doing poorly many months following operation. A third patient developed a constrictive pericarditis and required pericardectomy. There was one instance of adhesive pericarditis. In all of these, it was noted that the pericardium was accidentally opened at operation.

TABLE VI. COMPLICATIONS IN BRONCHOPLEURAL FISTULAS PRESENT STATUS ACCORDING TO SIDE AND TYPE OF OPERATION

	LOBE		PNEUMONECTOMY		TOTAL
	RIGHT	LEFT	RIGHT	LEFT	
Well	2	0	1	0	3
Sick					
Improving	1	3	3	1	8
Worse	1	1	2	1	5
Dead	1	1	8	1	11
Total	5	5	14	3	27

In Table VI it is noted that the incidence of bronchopleural fistula is much higher in the right pneumonectomies. This is attributed to the fact that the

TABLE VII. COMPLICATIONS

202 RESECTIONS FOR PULMONARY TUBERCULOSIS		
Spread and/or exacerbation		
Following lobectomy		
Contralateral	8	
Ipsilateral	8	
		16
Following pneumonectomy		11
Total		27*

*Both ipsilateral and contralateral in 2 patients.

TABLE VIII. SPREADS OR EXACERBATIONS OF CLINICAL SIGNIFICANCE IN 202 RESECTIONS FOR PULMONARY TUBERCULOSIS

Resulting in death		
Associated with bronchopleural fistula	11	
Without fistula	1	
		12
Continuing morbidity		
Growing worse	5	
Improving	8	
		13
Total		25

TABLE IX. PRESENT STATUS IN 202 RESECTIONS FOR PULMONARY TUBERCULOSIS

	NUMBER	PER CENT
Home	120	59.4
Hospital	57	28.2
Dead	25	12.4
Total	202	100.0

TABLE XI. DEATHS IN 202 RESECTIONS FOR PULMONARY TUBERCULOSIS

	LOBECTOMY	PNEUMONECTOMY	TOTAL
Postoperative	2	12	14
Late	4	7	11
Total	6	19	25

TABLE XI. DEATHS ACCORDING TO INDICATION FOR OPERATION

	NUMBER OF OPERATIONS	DEATHS	PER CENT
Thoracic failure	71	9	12.7
Bronchostenosis	33	4	27.1
Tuberculoma	26	0	0
Lower lobe disease	22	5	22.7
Mistaken diagnosis	22	4	18.1
Bronchiectasis	14	1	7.1
Not suitable for thoracoplasty	9	0	0
Destroyed lung	4	1	25.0

left bronchial stump is retracted to a more protected position beneath the aortic arch and buried in mediastinal tissue.

Transbronchial spread of disease or exacerbation of disease was the next most frequent complication and was frequently associated with bronchopleural

TABLE XII. CAUSES OF DEATH

	EARLY	LATE
Cardiac arrest	1	
Hemorrhage	3	
Shock	1	
Transfusion reaction	2	
Pulmonary insufficiency	4	
Progressive disease without fistula	1	
Bronchopleural fistula with empyema and progressive disease	2	9
Pericarditis		1
Nontuberculous disease		1
Total	14	11

TABLE XIII. SURVIVAL PERIOD

Six months or less	17
6 to 18 months	71
1½ to 2½ years	48
2½ to 3½ years	26
3½ to 4½ years	13
Over 4½ years	2
Total	177

TABLE XIV. PRESENT SPUTUM STATUS

	NUMBER	PER CENT
Negative (culture)	150	84.75
Positive	27	15.25
Total	177	100.00

fistula. It occurred in 14, or 14 per cent, instances in the lobectomy group with equal distribution between the two sides. It followed pneumonectomy in 11, or 10.5 per cent. In 2 patients spread or exacerbation occurred on both sides.

Further analysis of spreads or exacerbations of disease reveals that 12 results in death, 11 of which were associated with bronchopleural fistula. Thirteen were responsible for continuing morbidity. Of the 13 living patients in whom spread occurred, 8 are improving and 5 are becoming worse.

The following miscellaneous group of complications was encountered:

Tuberculous infection of chest wall	1
Chest wall sinuses	2
Wound dehiscence	1
Contralateral spontaneous pneumothorax following pneumonectomy	1
Temporary paresis of left recurrent laryngeal nerve	1
Laryngeal stridor due to a subglottic inflammatory membrane	1
Ulceration of bronchial stump	3

RESULTS

Of 202 patients who had resection for pulmonary tuberculosis, 120, or 59.4 per cent, are home; 57, or 28.2 per cent, are still in the hospital, and 25, or 12.4 per cent, are dead.

There were 14 operative deaths, a fatality rate of 6.9 per cent and 11 late deaths, or 5.5 per cent.

TABLE XV. PRESENT CLINICAL STATUS
HOSPITAL

	LOBECTOMY	PNEUMONECTOMY
Clinically well and negative	15	13
Ill or incapacitated		
Negative with pleural complications	2	2
Negative, respiratory cripple		3
Positive		
Fistula, empyema and/or spread	5	3
Spread or exacerbation	5	1
Previous contralateral disease	1	1
Stump ulcer	1	1
Source not determined	1	3
Total	30	27

TABLE XVI. PRESENT CLINICAL STATUS

177 PATIENTS HOSPITAL		
Clinically well		
Negative	28	35
Ill or incapacitated		
Negative with pleural complication	4	
Negative, respiratory cripple	3	
	—	35
Positive		
Fistula, empyema and spread or exacerbation	8	
Spread or exacerbation alone	6	
Previous contralateral disease	2	
Stump ulcer	2	
Source not determined	4	
	—	22
Total		57

TABLE XVII. PRESENT CLINICAL STATUS
HOME

	LOBECTOMY	PNEUMONECTOMY
Clinically well		
Negative	59	53
Negative with pleural complications		1
Occasional positive culture	2	
Ill or incapacitated		
Negative, respiratory cripple		2
Positive	1	2
Total	62	58

TABLE XVIII. PRESENT CLINICAL STATUS

177 Patients HOME	
Clinically well	
Negative	112
Negative with pleural complications	1
Occasional positive culture	2
Ill or incapacitated	
Negative, respiratory cripple	2
Positive*	3
Total	120

*Source: contralateral disease, 1; stump ulcer, 1; not determined, 1.

Of 104 pneumonectomies, 19 are dead, a total fatality rate of 18 per cent, whereas in the lobectomy group only 6 are dead, a total fatality rate of 6.1 per cent.

Table XI, which records the deaths according to indications for operation, reveals fatality rates near the mean figure of 12.4 per cent for; thoracoplasty failure and bronchostenosis. There were no fatalities in the tuberculoma group or in the group thought unsuitable for thoracoplasty. In the other categories fatality rates are distorted by the small number involved and are not statistically significant.

The causes of death are listed in Table XII.

As noted previously bronchopleural fistula and empyema in association with progressive disease was the most significant single factor in the fatality statistics, accounting for almost one-half of the deaths. This serves to emphasize again that the ultimate fate of the patient is largely determined by the status of the bronchial stump.

One death was due to cardiac arrest, 3 to hemorrhage, and 1 to shock. Two patients died as a result of transfusion reactions. In 4 pulmonary insufficiency was considered the cause of death. One patient died following pericardectomy for constrictive pericarditis. She also had a previously undiagnosed mitral stenosis. One death resulted from early massive spread without fistula. One late death occurred as a result of nontuberculous disease.

The time elapsed since operation is indicated in Table XIII. A majority of the patients have been operated upon within the past three years.

Table XIV records the present sputum status of 177 patients.

Tables XV, XVI, XVII, and XVIII show the present clinical status of living patients. Follow-up has been possible in all patients. It will be noted that of the patients now in the hospital nearly all of those listed clinically well and negative can reasonably be expected to move into the same classification in the home group. The fate of the positive group is predictable only in so far as those with bronchopleural fistula and progressive disease are concerned. It is estimated that at least 5 of these will die. The fate of the remaining patients is indeterminate, though it seems likely that most of them will live and several may become clinically well and negative.

Of 202 patients who had resection for pulmonary tuberculosis, 120, or 59 per cent, are home; 112, or 55 per cent, being clinically well and negative. Estimated on the basis of 177 living patients, 68 per cent are home, clinically well and negative.

DISCUSSION

There is little difference of opinion as regards the indications for resection except in the upper lobe lesions in which thoracoplasty would ordinarily have been employed. However, certain types of lesions have proved resistant to collapse by thoracoplasty and consequently are thought to be better treated by resection. The following types of lesion are representative of those in which resection is preferable to thoracoplasty.

1. Tension cavities. Thoracoplasty is frequently ineffective in closing tension cavities even when carried out with streptomycin to control associated bronchial disease and stenosis. Because of inability to predict a satisfactory response to thoracoplasty resection is frequently considered preferable.

2. Lesions which appear in the roentgenogram as scattered nodular infiltrates with fibrosis and indistinct areas of rarefaction suggesting small cavities, whether extensive or occupying a limited area. These lesions, the familiar fibrocaseous adult lesion, are usually found to be firm and inelastic and represent multiple areas of poorly encapsulated caseation with interspersed fibrosis. There is almost always demonstrable one or more small liquified areas of caseation which communicate with a small bronchus. Such lesions are very frequently much more extensive than their radiologic appearance would suggest and are resistant to any form of collapse.

3. Lesions so situated within the lobe as to require extensive thoracoplasty with needless sacrifice of pulmonary function.

4. Some giant cavities, especially in the gutter.

5. Progressive caseous pneumonic disease in children or young adults limited to an upper lobe. In fact, in all children resection is preferable to thoracoplasty.

6. Tuberculoma or tuberculoma-like lesions, in themselves prime indications *for resection whenever localized to a lobe or segment should never be subjected to* thoracoplasty or other collapse measures when located in an upper lobe. With very few exceptions these lesions should be resected. Even the presence of calcium is not always an indication of their benignity either from the standpoint of tumor or tuberculosis.

The lower lobe lesion, which has not responded well to collapse measures, is a logical indication for resection. It is questionable whether resection should be delayed for any but the briefest trial of other measures if the lesion is extensive. Obviously smaller infiltrates without cavity or larger exudative infiltrates which tend to clear should have a longer trial of bed rest and collapse before the decision is made to resect. Such obvious indications as the persistence of a lesion with positive sputum, evidence of associated bronchiectasis, tension cavity, filled cavity, or the presence of single or multiple encapsulated caseous foci, will dictate resection.

There is still another group of patients in whom the need for resection is anticipated but who, for one reason or another, should have thoracoplasty as the primary procedure. The prime example of this situation is the extensively involved lung or upper lobe in a patient who is in precarious immunologic balance. Thoracoplasty in such a situation will often throw the balance in favor of the patient and set the stage for resection. Thoracoplasty may in some instances even prove effective in controlling such lesions. Thus a sequence of events will have transpired which will render resection less hazardous and even in a few instances unnecessary.

A further benefit is thought to accrue as a result of this plan by reducing the space available for occupancy by the remaining lobe or lobes if a lobectomy has been done or making an empyema a less serious complication in the event that infection supervenes or the bronchus opens following pneumonectomy.

One of the most important factors determining the success of resection in pulmonary tuberculosis is adequate healing of the bronchial stump. Failure of healing in the early postoperative course, if not attributable to ineffective closure or streptomycin resistance, may be due to mucosal disease, though numerous instances have been noted in which adequate healing occurred when transection was carried through grossly diseased mucosa. The late occurrence of fistula would seem to be related to contiguous infection in the pleural space. The latter can be minimized by avoidance of gross contamination whenever possible by carrying the dissection into the extrapleural plane. However, contamination is unavoidable in many instances despite the most skillful manipulations and probably occurs much more frequently than is apparent from gross inspection.

The fear of streptomycin resistance has been lessened by experimental and clinical evidence that the combination of PAS and streptomycin has successfully delayed or prevented the development of emergence of significant resistance. This is particularly important in cavitary lesions which often require resection. Closer cooperation between medical and surgical departments in the management of antibiotic therapy in the acutely ill patient in preparation for later surgery should result in fewer resistant patients and consequently render surgery less hazardous in this salvage group.

That further expansion of the area of usefulness of resection will occur is quite likely. However, thoracoplasty continues to be a highly effective measure for the control of a large number of upper lobe lesions and will probably maintain a prominent if not the commanding position it has enjoyed as the most universally effective major surgical procedure. Its limitations as regard the control of certain types of lesions must be more clearly defined. A better correlation of the radiologic appearance with the pathologic characteristics of the lesion should be the basis for selection of the appropriate procedure.

SUMMARY

The results of resection in 202 patients with pulmonary tuberculosis have been presented. There were 98 lobectomies and 104 pneumonectomies.

Bronchopleural fistula with empyema occurred in 27, or 13 per cent, of the patients and was the major cause of death. Spread or exacerbation of disease occurred in 14 per cent of the lobectomies and 10.5 per cent of the pneumonectomies.

Fourteen patients died following operation and eleven died later, a total fatality rate of 12.4 per cent. One hundred and seventy-seven patients are living six months to five years following operation. One hundred and twenty, or 68 per cent, of these are home and clinically well.

One hundred fifty, or 85 per cent, of the survivors have negative sputum or gastric washings on culture.

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(See discussion on page 875.)

LOBECTOMY AND PNEUMONECTOMY IN THE TREATMENT OF PULMONARY TUBERCULOSIS

A TEN-YEAR SURVEY

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INTRODUCTION

PULMONARY resection is a method of treatment of tuberculosis which has gained increasing attention in the past several years. The report of Churchill and Klopstock[1] indicated the potential use of the procedure. The reports of Maier[2] and Sweet,[3] in 1946, indicated that early results deteriorated in the later follow up and Sweet[4] recently has reported his group again "as showing that extirpative surgery is a procedure of limited usefulness in the management of the disease." Overholt and his group[5,6] have demonstrated the results in a considerable series of patients. Their experience covers the period since 1934, and they have added the use of streptomycin and upper thoracoplasty in their later cases. Their reports stress the good results, particularly in the face of difficult problems of therapy and several reports[7,8,9,10] have indicated the value of streptomycin in the preoperative and postoperative period. This study was undertaken at Bellevue Hospital to evaluate our experiences for further use of the procedure.

MATERIAL

The seventy-three cases in this report include all patients on the Bellevue Hospital Chest Surgical Service in the period 1939 to October, 1948, on whom a resection was done for pulmonary tuberculosis. The records of the pathology department were reviewed and all surgical specimens of lung tissue in which a diagnosis of tuberculosis was made were checked against the former group. The charts were then reviewed and if tuberculosis was not of clinical significance, the cases were omitted from this study. Four cases from the Chest Surgical Service of the Veterans Administration Hospital, Bronx, N. Y., are included.

An attempt was made to follow all patients at regular intervals and an effort to review all of the group was made recently. Two have never returned for a follow-up visit.* The remainder were seen by one of the authors during 1950, or recent roentgenograms were reviewed and present status determined by letters from their physicians.

Lobectomy was performed on forty-two patients and thirty-one had a pneumonectomy. There were twenty-eight upper and fourteen lower lobe

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*The patient with pneumonectomy was located recently and a roentgenogram seen. She has endobronchial disease in the remaining lung.

resections, and seventeen right and fourteen left pneumonectomies. One classified as a pneumonectomy had only ligation of a vessel; resection was abandoned because of poor condition at that time, and death occurred on the forty-eighth postoperative day. Once pneumonectomy was performed three years after a tourniquet lobectomy for bronchiectasis because of the development of tuberculosis in the residual stump of lung. There were no segemental resections. In most instances the operator was the resident thoracic surgeon, although a member of the attending staff was always present and decided on the advisability and the extent of the pulmonary resection. The cases were fairly evenly distributed among the ten members of the attending staff.

RESULTS

Lobectomy.—In Table I a summary of the results in the lobectomy group is given listing the year each patient was operated upon. The results are classified by groups: clinically well, alive with active disease, died. The thirty-one listed as clinically well have negative sputum and developed no new lesions in the follow-up period. Two patients included in this group showed a minimal exacerbation of old lesions which promptly subsided and have remained unchanged for at least two years. Four in the group are alive with active disease; one developed a cavity in the lower lobe on the operated side, the others have new infiltrates which appeared after two years of observation. There were six deaths. One patient was not followed.

The indication for operation is given in the subheadings. Lobectomy was undertaken as the primary method in the first group. In the second, thoracoplasty was performed. The disease later progressed and excavated under the collapse. Six months to several years followed the original operation before resection was undertaken. The third group includes those for whom a thoracoplasty and lobectomy were planned before either procedure was undertaken. The collapse was the first operation in one-half of these. When it followed resection it usually was done two to three weeks later. These were all four or five-rib posterior thoracoplasties leaving transverse processes in place and in a few, the first rib was not removed. Scoliosis was not seen in the group. There were several patients in the first and third groups on whom thoracoplasty might have been tried as a sole therapeutic method for upper lobe disease. In a case by case review of the material, we believe that the results obtained so far by combining limited thoracoplasty with resection and streptomcyin have been as good or better than might have been anticipated in the same period by the use of collapse therapy alone.

Twelve lobectomies were done prior to 1947. More recently, after streptomycin became available, it has been given to all patients undergoing resection when tuberculosis was diagnosed. Ten of fourteen patients had a thoracoplasty in an attempt to prevent overdistention after upper lobe resection. The question of thoracoplasty arose in the others only after the histopathologic report on the resected specimen showed tuberculosis. Since the lungs then were well expanded and presumably adherent, it was felt that thoracoplasty would collapse a small segment and leave the remainder of the lung distended. After lower lobe lobec-

TABLE I. RESULTS IN 42 LOBECTOMIES FOR PULMONARY TUBERCULOSIS

		TOTAL	1948	1947	1946	1945	1944	1943	1942	1941	1940	1939
Lobectomy no thoracoplasty	Not followed	1		1								
	Clinically well	11	5[A]	2[B]			2		1			1
	Alive with active disease	2	2[C]									
	Died	4				1	1	2				
Lobectomy for thoracoplasty failure	Clinically well	11	3	5				2		1		
	Alive with active disease	2	1	1								
	Died	1								1[E]		
Planned[d] lobectomy and thoracoplasty	Clinically well	9	8	1								
	Alive with active disease	0										
	Died	1	1									

[A] Four were lower lobe resections one of which had a phrenic crush.

[B] One was lower lobe resection.

[C] One patient had a phrenic crush after lower lobe lobectomy.

[D] One thoracoplasty after lower lobe lobectomy consisted of removal of ribs seven to ten, two were ribs two to four, the others were upper four or five rib thoracoplasties.

[E] Patient died in 1945.

TABLE II. CAUSES OF DEATHS IN 6 PATIENTS AFTER LOBECTOMY FOR TUBERCULOSIS

DATE OF LOBECTOMY	TIME OF DEATH	COMMENT	CAUSE OF DEATH
1941	4 years	Tourniquet lobectomy LLL for tuberculosis. Developed bronchopleural fistula, empyema, and slowly progressive pulmonary tuberculosis	Extensive tuberculosis
1943	22 months	Lobectomy undertaken with diagnosis of lung abscess. Specimen showed fibrocaseous tuberculosis with cavitation. Died in sanatorium. Autopsy showed widely disseminated tuberculosis	Extensive tuberculosis
1943	18 days	*Lobectomy for tuberculosis, large tension cavity which emptied suddenly on operating* table, inundating airway. Massive bilateral spread and bronchopleural fistula. Autopsy: tuberculosis in wound, pleura, lung, appendix	*Extensive tuberculosis*
1944	50 days	Lobectomy for large tuberculosis cavity. Disease tissue sectioned at operation Postoperative bronchopleural fistula, bilateral spread, and terminal hemoptysis	Extensive tuberculosis and hemoptysis
1945	3 hours	Lobectomy for suppurative disease, specimen showed cavity with fibrocaseous tuberculosis. 3 preoperative cultures for tuberculosis returned positive postoperatively Autopsy: fibrocaseous tuberculosis in opposite lung. Cause of death, hemorrhage *into pleural cavity*	*Hemorrhage*
1948	1 year	Upper lobe tuberculosis, pneumothorax, pneumolysis, acute empyema, and bronchopleural fistula following lysis. Admitted to Bellevue. Drainage upper thoracoplasty, streptomycin, drained. Lobectomy and decortication, localized empyema in apex of chest. Progressive tuberculosis of anterior chest wall, lungs clear. Depression. Inanition	Extensive pleural tuberculosis

TABLE III. RESULTS IN 31 PNEUMONECTOMIES FOR PULMONARY TUBERCULOSIS

		TOTAL	1948	1947	1946	1945	1944	1943	1942	1941	1940	1939
Endobronchial tuberculosis	Not followed	1		1								
	Clinically well	6	2	1	1		1[A]			1		
	Alive with active disease	0										
	Died	2									1	1
Extensive unilateral disease	Clinically well	6	4	1	1							
	Alive with active disease	1	1									
	Died	4	4									
Thoracoplasty failures	Clinically well	2	1				1[B]					
	Died	1										1
Diagnosed tumor preoperatively	Clinically well	3	1	1			1					
	Died	1		1								
Suppurative disease eroding tuberculous focus	Alive with active disease	1	1									
	Died	1					1					
Schede failure	Clinically well	1	1									
Lobectomy for bronchiectasis in 1944. tbc in remaining lobe.	Clinically well	1		1								

[A] Questionable activity that cleared in remaining lung.

[B] Thin walled cavity with negative sputum that cleared rapidly—? Emphysematous bleb.

TABLE IV. CAUSE OF DEATH IN 9 PATIENTS AFTER PNEUMONECTOMY FOR TUBERCULOSIS

DATE OF PNEUMONECTOMY	TIME OF DEATH	COMMENT	CAUSE OF DEATH
1939	48 days	Severe tuberculous bronchiectasis with suppuration and positive sputum. Only procedure was ligation of one vessel. Operation abandoned, because of uncontrolled secretions. Developed massive spread	Massive spread
1939	2 days	Patient poor functional risk. Lobectomy planned, pneumonectomy necessary. Very stormy postoperative course with marked respiratory difficulty and bronchiogenic spread to opposite side	Respiratory failure and spread
1940	6 days	Long history of tuberculosis, empyema, BPF, drainage, and complete thoracoplasty. Pneumonectomy followed by massive spread	Massive spread
1944	6 days	Quiescent Friedlander pneumonia, bronchiectasis, and fibrocaseous tuberculosis preoperative. Postoperative massive Friedlander's spread with fibrocaseous tuber*culosis in other lung.*	Massive Friedlanders and tuberculosis
1947	10 days	Diagnosed as Ca. preoperatively. Fibrocaseous tuberculosis in lung. Bronchopleural fistula, empyema, and massive spread	Massive spread with Bronchopleural fistula
1948	1 month	Borderline functional risk. Lobectomy planned, pneumonectomy done because of technical difficulties. Survived stormy postoperative course, then did well. Died 2 days after thoracoplasty of respiratory failure	Respiratory failure
1948	5 days	Patient had extensive unilateral disease and laryngotracheal disease controlled with streptomycin. Postoperative tracheotomy necessary. Died suddenly from apparent blockage of airway. Section from trachea showed acute edematous swelling and acellular membrane formation	Asphyxia after tracheotomy
1948	2 days	Extensive unilateral tuberculosis. Uneventful pneumonectomy. Developed pulmonary edema with high Hct and Hgb, probably result of overtransfusion.	Pulmonary edema
1948	3 weeks	Extensive disease. Period of cardiac arrest at operation. Followed by marked evidence of cerebral damage. Never recovered consciousness. *No tuberculosis* found in opposite lung	Cerebral anoxia *with extensive* brain damage

each patient is considered individually. The group of patients who had pneumonectomy reflect a more extensive disease by a higher mortality. In reviewing these cases, it was difficult to visualize any other form of therapy that would adequately have controlled the disease. When the indication was extensive unilateral disease, it was noted in the pathology report that caseation was present in many areas. In reviewing the group that is listed as thoracoplasty failures, it is brought out that most of these result from caseous disease which continues to excavate in the area under collapse. Initial resection offers a much more favorable outlook in such lesions.

After pneumonectomy, thoracoplasty has been done routinely leaving the first rib in place and with limited resection of the posterior segments. Scoliosis is seen infrequently after this procedure.

These patients were all seen in a general hospital where pulmonary suppuration is not an uncommon disease. Several patients included in this report were operated upon with this diagnosis. In a few of these the process was tuberculous and was undiagnosed. We now have had a considerable experience with acute lung abscess which occurs in an area adjacent to quiescent tuberculosis and as the process extends and invades the tuberculous area, the sputum becomes positive and the copious secretions form an excellent vehicle for spread. The combination of suppurative disease and tuberculosis in the same lobe is a strong indication for resection.

SUMMARY

1. Seventy-three cases of pulmonary resection for tuberculosis in the period 1939 to October, 1948, are presented.
2. Lobectomy combined with thoracoplasty and streptomycin gave the most satisfactory follow-up results.
3. The indications for lobectomy were discussed. Poor results in the late follow-up period need not be anticipated. There remains a group in whom thoracoplasty or lobectomy offers a considerable chance for improvement. The choice of procedure must be individualized.
4. Pneumonectomy usually was undertaken for far-advanced lesions and the high mortality is not a contraindication for its continued use.

CONCLUSION

In conclusion, it seems evident that there are many patients in whom thoracoplasty and resection may be anticipated to offer the best opportunity for control of the disease.

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DISCUSSION ON "FURTHER EXPERIENCES WITH SEGMENTAL RESECTION IN TUBERCULOSIS" BY DR. J. MAXWELL CHAMBERLAIN AND DR. ROBERT KLOPSTOCK;* "RESECTION IN THE TREATMENT OF PULMONARY TUBERCULOSIS" BY DR. J. CLAUDE DAY, DR. W. M. TUTTLE, DR. E. J. O'BRIEN, DR. FOSTER HAMPTON, JR., AND DR. TRUXTON L. JACKSON,† AND "LOBECTOMY AND PNEUMONECTOMY IN THE TREATMENT OF PULMONARY TUBERCULOSIS" BY DR. AARON HIMMELSTEIN, DR. FRANK B. BERRY, AND DR. C. THOMAS READ

COL. JAMES H. FORSEE, Denver.—Prior to 1947, it was our belief that pulmonary resection in tuberculosis was seldom indicated except for thoracoplasty failures and in certain instances of bronchial stenosis. Beginning in 1947, and with the advent of adequate quantities of streptomycin, we have carried out lobectomy in a consecutive series of 94 patients, with a mortality rate of 2.1 per cent. Reactivation or spread of the disease has occurred in five patients, bronchopleural fistula in five, and empyema in three patients. In an over-all summary of 124 patients treated during the period 1947 through 1949, on whom pulmonary resection was performed as pneumonectomy, lobectomy, segmental or partial lobectomy, the over-all mortality to date is 4 per cent.

We believe it important to carry out upper stage thoracoplasty of five ribs, either preceding or at the same time lobectomy is performed. Of extreme importance and only to emphasize its significance, is the importance of teamwork in caring for such patients, including the internist, endoscopist, and pathologist. Our most important recent contribution has been the work carried on by Colonel Temple and his co-workers at Fitzsimons in a study of streptomycin resistance. Briefly, in a group of 100 patients who have been treated with streptomycin for a period of 120 days, in dosages of 1 or 2 Gm. every third day, combined with para-aminosalicylic acid 12 Gm. daily, one-third have completed the study and have had resistance studies made. To date, there has been no instance in which sensitivity has not been retained in the 33 patients. The other 67 have completed their course of streptomycin and PAS therapy, but resistance studies are not complete. This is particularly important to the surgeon in that if the patient who undergoes pulmonary resection is sensitive to streptomycin he is a better risk and has a better chance for ultimate recovery. The one common denominator since 1947 which has made pulmonary resection such an adequate measure in the management of pulmonary tuberculosis is, in our minds, streptomycin.

DR. ANTHONY R. CURRERI, Madison, Wis.—While in the main I believe we agree with the philosophy of Dr. Chamberlain, I think many of us might take exception to one point that he has made; that is, that one can tell by x-ray examination all of the active tuberculosis present in the lung. This is not true, because in our series, by correlating roentgenograms and planograms to the surgical and pathologic findings, we noted that many lesions not seen in the x-ray examination became apparent on surgical exploration, and active infection was demonstrated by lung sectioning and microscopic and bacteriologic studies.

Furthermore, in our first series of 80 cases, segmental resection was carried out in 4 cases, two of these developing bronchopleural fistula and a third had excessive pleural effusion. We decided, therefore, that segmental resection should be resorted to when mandatory be-

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*See page 843 for article by Chamberlain and Klopstock.
†See page 854 for article by Day, Tuttle, O'Brien, Hampton, and Jackson.

cause of inadequate pulmonary reserve. Our results are in complete agreement with Dr. Berry's and Dr. Himmelstein's. We wish to compliment Dr. Day and his co-workers in focusing our attention on the possibility of major complications, particularly bronchopleural fistula that may be associated with resection. However, we are convinced from our own studies, in which some cases have now gone over five years, that in properly selected cases pulmonary resection has a definite place in surgical treatment of tuberculosis, should be attended with excellent results and few complications.

In April, 1948, Dr. Gale and I reported 80 consecutive resections for tuberculosis. We have continued to follow these cases closely, and in addition have performed another 120 resections up to November, 1949. May I show three slides demonstrating the results of these cases?

(Slide.) You will note that in our original report of April, 1948, 42 per cent of the patients were sputum negative but still in a sanatorium, 31 per cent were negative and at home, and 22 per cent were positive. By September, 1949, one and one-half years later, there were but 12 per cent that were sputum negative and still in a sanatorium, while another 63 per cent were negative and at home—indicating that 75 per cent had converted and the vast majority were at home. Fifteen per cent of the patients were still positive. Our original 1948 series showed two deaths attributable to the operative procedure. Three more died from unrelated causes. In the ensuing two years two more patients have died from causes other than tuberculosis, making a total of seven deaths from the original series of 80.

(Slide.) This shows the stability of sputum conversion. Note that in the original report sputum conversions were under eighteen months, while eighteen months later the vast majority of patients have been tubercle free for well above twenty-four months, with a fair number free of tubercle bacilli for four to five years.

The third slide presents our surgical indications and the mortality of the original group as compared to the second group of 120 resections performed between April, 1948 and November, 1949. Whereas thoracoplasty failure and bronchial stenosis accounted for approximately three-fourths of our indications in the first group, in the second group the picture changed, with bronchiectasis the indication in 35 per cent, thoracoplasty failure in 27 per cent, and bronchial stenosis in 6 per cent. There were five operative deaths in the second series, about double the original group. This increased mortality is partly our fault, for with increasing success we accepted patients with extensive bilateral disease or those resistant to streptomycin and still having evident tracheobronchitis. Further, streptomycin deceived us in several cases for, despite the apparent subsidence of bronchitis as manifested by a healing mucosa, section of the bronchus at the time of surgery revealed a cheesy submucosa. Obviously the selection of such cases resulted in a high incidence of respiratory cripples and bronchopleural fistulas. There were three respiratory cripples, one of whom died, and nine bronchopleural fistulas. A lesson was learned from the bronchopleural fistulas in that we attempted to close the blown bronchial stump in five cases, and four of these died. The remaining four had immediate drainage performed, followed by thoracoplasty. Three of these have spontaneously closed their fistulas.

DR. JOSEPH GORDON, Ray Brook, N. Y.—I should like to bring to you some information that has been helpful to us, which does not include a series of cases. At Ray Brook we have continued with our studies of the removed lung specimens by injecting the pulmonary artery and the bronchial tree and carefully studying these specimens for the extent, distribution, and type of pathologic change which is present. With these studies as the base line we feel that we have a better method of evaluating bronchography. We believe bronchography has reached the point where it is extremely helpful in eliciting the structural changes present in the lung before embarking upon surgical planning of these cases.

(Slide.) Here you see on the left the x-ray film of a markedly destroyed lung on which pneumonectomy was done. The film following it is that of an arteriogram of the pulmonary artery showing marked destructive changes in this area. The film following that is the bronchial tree injected, showing the alteration in the bronchial tree. These, as we mentioned last year, show changes both in the pulmonary artery and in the bronchial tree in tuberculosis. It is these changes that correlate so well with the distribution of disease that we have used them as a basis for bronchographic interpretations.

(Slide.) Here you see what looks like a moderately diseased lung on the left side, but the bronchogram shows an extremely poor pattern and this is a relatively nonfunctioning lung. The bronchial pattern reveals areas of extensive structural changes by absence of arborization with shortening and widening of the bronchial tree.

(Slide.) Here is an x-ray film which shows moderate disease, the location of which is not accurately indicated except that we see it is rather extensive. The bronchogram on the right shows that the upper lobe is involved as well as the apical segment of the lower lobe. The remaining portion of the lung has a relatively normal bronchial tree and we therefore feel that the attack on this should be localized to the areas of abnormal bronchograms.

(Slide.) This is the post re-expansion bronchogram in a case in which there is no function in the lung. The bronchial tree shows the same marked alteration, absence of arborization, shortening and widening.

(Slide.) The x-ray film shows disease on the left in the region of the upper lobe and a portion of the lower lobe; the bronchogram shows that the disease in the upper lobe is rather widespread and only the apical portion of the lower lobe is involved; the remaining portion of the bronchial tree is normal, so we could confine resection to the upper lobe and apical portion of the lower lobe.

(Slide.) This is a similar case; the same abnormal changes in the bronchial tree.

(Slide.) This case shows the contrast; there is a giant-sized cavity in the apex of the lower lobe; the bronchogram, however, is abnormal throughout, and it would be inadvisable to attempt a segmental or lobe resection, because the entire lung is involved and must be so treated.

(Slide.) This shows abnormal changes in bronchogram in the presence of involved lung.

(Slide.) This is the most striking case of all, of a patient who had minimal disease in March, 1949, then developed pneumonic type of disease in July, 1949, of the right upper lobe, for which the patient was treated with streptomycin. There is marked regression of the abnormal shadows. The interpretation is extensive clearing. However, the bronchogram shows rather extensive alteration of all segments of the upper lobe.

DR. ROBERT GLOVER, Philadelphia.—I should like to congratulate the essayists on their very excellent presentations and results, and particularly Dr. Chamberlain for undertaking this interesting and important work, for the courage it took and also his excellent results.

(Slide.) Two years ago we were privileged to present before this Association a series of 200 consecutive cases of resections for pulmonary tuberculosis. This series started in 1941, and terminated early in 1948. The slide presents an initial series of 100 cases with a mortality rate of 27 per cent; those cases did not have the benefit of streptomycin. The next 100 cases had the benefit of streptomycin and the mortality rate was reduced to 16 per cent.

(Slide.) We have extended this series to include 347 cases to the first of this year. There have been 58 deaths in the entire series, which represents an over-all mortality of 16 per cent. There have been an additional 20 deaths in the postoperative period to date, bringing the entire mortality up to 22 per cent. Living at the present time are 269 cases. Within the past three months we have endeavored to carry out a very extensive follow-up and have been able to contact each patient. We find that of the original 347 cases, at the present time there are 242 negatives, representing approximately 70 per cent of the entire series. There are 27 positive cases, or 7.7 per cent.

DR. WILLIAM M. TUTTLE, Detroit.—It seems rather interesting that Dr. Chamberlain has been able to gather together such a large group of segmental resections in the treatment of tuberculosis. This is especially so in view of the fact that there have been relatively few segmental resections done in a combined series of almost 800 resections reported here today. While Dr. Chamberlain did not have an opportunity to demonstrate by lantern slide the type of lesion to which he applies segmental resectional surgery, one is forced to assume that in some instances these patients might have been adequately treated by simpler collapse measures.

In reference to our own series and to the others reported here today it becomes evident that we have, I believe, not taken into consideration to a sufficient degree why patients after resectional surgery die either early or late. In our group it is quite evident that the majority of our deaths occurred as a result of the opening either early or late of the bronchial stump. It is likewise interesting that the majority of these stump openings occurred on the right side where the stump is more difficult to bury. This, I believe, fits in well with the observations of Dr. Rienhoff, which were made many years ago, namely, that a well-buried bronchial stump in the experimental animal seldom opens. The various series reported here today would remind us again that adequate bronchial closure still presents a problem.

DR. LOUIS R. DAVIDSON, New York.—I should like to echo Dr. Glover's complimentary remarks relative to the essayists. The very interesting paper of Dr. Day I agree with almost completely, but I should like to take this particular exception. If there ever was an indication for excisional surgery it is in the destroyed lung. Perhaps I did not hear Dr. Day correctly, but I feel that that is, beyond the shadow of doubt, one of the most important indications for excisional surgery.

Between March, 1946 and December, 1948, at Seaview Hospital, 200 resections for pulmonary tuberculosis were performed by 15 operators. Most of the surgery was done by the resident staff. There were 157 pneumonectomies, 38 lobectomies on 32 patients, and 13 segmental resections on 11 patients. During 1949, these cases were screened and classified rather intensively by reviewing the history, laboratory findings, x-ray studies, surgery, and pathologic material. In addition, most of the cases were seen in the follow-up clinic. One hundred ninety-two of the 200 specimens were evaluated; in a certain few instances we were of the opinion that excessive tissue had been removed when pneumonectomy was performed. Among our conclusions, it was believed that most pressing needful conditions demanding excisional surgery, were previous surgical failure, mixed infections, tuberculous empyema bronchopleural fistula, and a destroyed lung. Our ideas concerning the status of the contralateral lung or the remaining ipsolateral lung, and their relationship to surgery, have been altered during these years, particularly because of our study of these pathologic specimens. We like to call the arrested type the encapsulated caseous foci, and we think the contralateral lungs as shown in the films play no part in the consideration for surgery, if there is a stable lesion that has been present for a substantial period of time.

(Slides.) This patient was operated upon about 25 months ago; a pneumonectomy was performed. (Slide.) This shows the condition in January of this year; he is in good health and doing very light work.

Of Total 200 Patients

151 alive and sputum negative	75.5%
9 alive and sputum positive	4.5%
40 deaths	20.0%
29 bronchopleural fistulas	14.5%
6 empyemata	3.0%
17 sinuses and wound breakdown	8.5%
7 tuberculosis spreads	3.5%

DR. JULIAN A. MOORE, Asheville, N. C.—I should like to congratulate Dr. Chamberlain on his excellent results, but I cannot agree that segmental resection has as yet replaced thoracoplasty. I think after a period of five years if the results remain good it may prove his point. We have done only a few segmental resections without any mortality rate; have had two spreads of the disease at a later period following segmental resection. We have now done at Oteen more than 200 resections, and we have more complications. The trouble comes from two sources. We are beginning to get late fistulas, late empyemas, late spreads. So we do not know what the final result will be. However, the complication rate is greater in those patients who have been treated with streptomycin before they came to surgery. We are getting very few patients who have not received streptomycin, and the complication rate has doubled.

Where we are able to control the administration of streptomycin a little better our complication rate remains low. I am rather appalled in private practice at seeing so few patients with tuberculosis who have not been given streptomycin at the beginning of the disease. At this rate, five years from now, the tuberculous population of this country will be streptomycin-resistant. I feel that its use should be confined to definite indications and that it should not be given indiscriminately. I am also certain that streptomycin is still a protective agent and an adjunct particularly to resection and major collapse measures.

DR. JOHN JONES, Los Angeles.—I thought it might be of some interest to you to see a recent study we have made of our cases, Dr. Robinson, my associate, and I. We have used essentially the same technique on these patients on the group operated upon between 1943 and 1949. In all, we had a mortality of 12.2 per cent in 123 resections; and in the group classified as collapse failure, we have 24 per cent mortality; in the destroyed lung group we had 40 per cent mortality; and in that smaller group of 32 patients where the operation was purely elective we had no mortality and a fairly low incidence of complications.

(Slide.) What are the causes of these complications and the mortality? We found in the entire group that our greatest problem was spread of the disease, which accounted for 90 per cent morbidity, 5.7 per cent mortality; opening of the stump, 2.4 per cent mortality. The other causes were 1 per cent wound infection; two operative deaths, 1.6 per cent mortality.

(Slide.) If we compare the group operated on before we had streptomycin with those that had the advantage of streptomycin, we have the complication of empyema, for example. In the 35 patients who had no streptomycin, the mortality from empyema was 2.8 per cent, and an incidence of 11.4 per cent in the group of 35 patients. Still, in the group of 88 patients who had streptomycin, we had only 2.3 per cent morbidity, and no mortality from that one complication.

(Slide.) The opening of the bronchial stump was of course a common cause of mortality—8.6 per cent in a group of 35 nonstreptomycin patients, and still we had no bronchial fistulas in the 88 who had streptomycin.

(Slide.) The third complication was spread of the disease. We had 17 per cent of our patients die of spread of the disease in the small group of 35 nonstreptomycin patients, and still only 1.1 per cent in the 88 patients who had streptomycin. The technique was essentially the same; there were only two surgeons who operated upon these patients. All the bronchial stumps were closed with stainless steel sutures. We have here a total mortality of 5.7 per cent due to opening of the stump, all in the nonstreptomycin group.

(Slide.) Finally, if you group all the figures together, you will not have such a good mortality, 12.2 per cent; but if you look at the patients who had streptomycin you have a fairly respectable mortality of 5.7 per cent in 88 resections, but still an appalling mortality of 25 per cent in the 35 patients who did not have streptomycin, and more than 50 per cent morbidity in that small group. In reporting statistics on resections in tuberculosis it is, then, obvious that it is well to state whether the patients had the protection of streptomycin during their surgical treatment.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—There is no doubt that the incidence of bronchial fistula has been on the decrease since we have had chemotherapy, both in tuberculosis and in nontuberculous cases. I believe that safe bronchial closure is not only due to chemotherapy, it is also due to the technique with which the bronchial stump is closed. If there is not any naked cartilage left in the stump to be closed, and if the closure can be done with a continuous peripheral suture and invagination, the incidence of bronchial fistula will be very small, both with and without chemotherapy. In our early experience, resections both in tuberculous and nontuberculous cases, gave a very small incidence of bronchial fistula, and since 1945, when we got chemotherapy, I cannot remember any cases of bronchial fistula in my material.

With regard to the cases presented by Dr. Chamberlain and discussed by Dr. Tuttle, I believe that the type of tuberculosis we have in Sweden is quite different from the type you have in the United States. If we tried to close any of the cavities which Dr. Chamberlain has resected with phrenic nerve operation, as Dr. Tuttle advised, I do not believe we would get success in more than perhaps 1 or 2 per cent.

DR. NORMAN WILSON, Boston.—I also would like to congratulate the three essayists, and I think it is well for us to remind ourselves as we look at the statistics of the last two papers, that had they chosen to break them down into recent years, in the streptomycin era, their over-all figures wound have been much better, I rise merely to give you a late follow-up of a series of cases, and also what we consider to be the results in the modern era with everything we have to use.

In June of last year we were able to follow 100 per cent of living patients of the first 323 resections. Of this group 75 per cent were living; 80 per cent were classified by their own physicians as well in May. Sixty-six per cent of these patients were followed more than three years. The interesting point to us was, that of all the people who died of tuberculous infection, all save 10 had died of a progressive postoperative complication, or a complication related to a postoperative complication—in other words, fistula and spread. Only 10 people had died of an old progressive lesion, which would indicate that if we can carry these people through the operative period safely, their prognosis should be good.

In the last three years, with streptomycin and, I believe also, with more intelligent selection of patients, and, contrary to Dr. Tuttle's conception, with an increased application of segmental resection, I think we have been able to do a better job in many cases. In that period we have done 209 cases, 137 pneumonectomies, 48 lobectomies, and 24 segmentals. In the pneumonectomies, the tuberculous complications total has been 7 per cent; lobectomies, 2 per cent; segmentals, 4 per cent. Tuberculous deaths in pneumonectomies, 0.7 per cent; lobectomies, 0 per cent; segmentals, 0 per cent. The total tuberculous deaths, 0.5 per cent.

The nontuberculous deaths are increasing because our age groups are getting older. We have eight patients with pneumonectomies dead from a nontuberculous cause such as shock or coronary occlusion; we have 2 per cent lobectomy patients dead from nontuberculous causes; we have one segmental, who died of an embolus. I think these results should encourage Dr. Chamberlain to continue.

DR. CHAMBERLAIN (Closing).—First, may I make a correction; in the slide in which I showed the complications, I said there were three reactivations—there were actually five. These five are described in the manuscript. I did not mean to deceive you. Each reactivation and each death is explained in the text.

I should like to thank all the discussors for both their constructive and destructive criticism. Dr. Curreri spoke of the activity of foci; I thought I had pointed out in the text that there were three types of lesions left behind: (1) active ones, which I believe we all recognize from changes in the serial x-rays; (2) the indolent ones, in which the x-ray changes are so slight we cannot tell much about them; and (3) the arrested ones. It was also mentioned that all residual foci were treated as though they were indolent or smoldering foci, and therefore the patients were given six months bed rest after the resection. Dr. Curreri also suggested that the operation should be used only in patients with low respiratory reserve. From our present experience, the patient with a low respiratory reserve is not the type of case on which segmental resection should be tried. Segmental resection will rarely pull a bad risk patient out of a precarious functional situation; on the contrary, one slight complication, after segmental resection or any other procedure, may put the patient with a low respiratory reserve beyond the margin of safety. Our unfortunate results have been in patients who were considered poor risk patients for all other procedures as well. I don't know how to explain his three out of four failures in segmental resection. However, in the six bronchial fistulas which we have reported, three occurred almost consecutively; I am sure, had they been my first three cases I would feel as Dr. Curreri does. I can only say that he should give the procedure another trial, and perhaps his results will not be so unfortunate.

Dr. Tuttle surprised me by his discussion because I took this paper to Detroit and tried it out about nine months ago at the meeting of the National Tuberculosis Association. I believe Dr. Tuttle was in the audience when we showed the first 15 or 16 consecutive cases that we had done. At that meeting he held his tongue and so I thought I was safe in presenting it here today. He referred to the deaths. I think it was pointed out that the anesthetic death was the one case directly related to the operation and, under normal circumstances would have been considered a surgical death. The accident was simply this: At the end of the operation and after the patient was dressed and turned on his back, the anesthetist turned on the oxygen tank. The intratracheal tube was still in place and its balloon inflated. For some reason the reducing valve did not work and the patient received the entire pressure of the oxygen tank and blew up on the table. Death was immediate. Since we did not have an opportunity to find out whether he was or was not going to die from the operation, several of us felt that perhaps it was fair to call this an anesthetic death.

Dr. Tuttle pointed out also that in their 200 cases they have done no segmental resections; that the Madison group have done no segmental resections; and that in many other reports they have done no segmental resections. My only response to this observation is that in 1930 no one had done any resections.

Dr. Julian Moore made perhaps one of the most valuable comments. In my notes, which I did not have time to read, the last sentence states—"This operation is not a panacea, nor is it done without hazard, and it will require at least five years for real evaluation."

DR. DAY (closing).—I should like to thank all the discussors. Dr. Wilson has been so kind as to point out that we made no effort to separate the recent results from those of earlier years. Our recent results, of course, show lower fatality and morbidity rates than those for the total series.

I should like to thank Dr. Davidson for his kind remarks. We have been deeply concerned about the problem of the open bronchus. It is somewhat reassuring to know that we are not the only ones plagued by this problem. With regard to the destroyed lung, I think we are not particularly at variance with the opinion of Dr. Davidson and others. A large number of lungs which, perhaps, one would classify as destroyed were found to have high grade stenosis of the stem bronchus and were, therefore, included in the bronchostenosis group.

I should like to correct the impression that we have not done any segmental resections. Separate mention will be made of them in the manuscript. Though accompanied by more difficulties than the lobectomies, the results have not been too bad. I believe that Dr. Tuttle's criticism of Dr. Chamberlain is rather more severe than intended. I think Dr. Chamberlain is to be congratulated for his courageous attack on this problem. I am sure that Dr. Tuttle believes with the rest of us that segmenal resection will, indeed, play an increasingly important part in the treatment of pulmonary tuberculosis.

DR. HIMMELSTEIN (closing).—I would like to emphasize that our report includes cases operated on prior to the end of 1948, so that our shortest follow-up is about a year and one-half. The comments by Dr. Wilson hold for the cases we have seen; there has been one death in the lobectomy group since the use of streptomycin.

PULMONARY RESECTION IN TUBERCULOSIS: ITS HAZARDS, INDICATIONS, AND RESULTS

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THE extent to which any therapeutic procedure is used in the treatment of pulmonary tuberculosis is constantly modified by the results obtained. This is especially true in the early years of the development of a new surgical measure. Time and experience are required for the perfection of the technique and for the recognition and modification of the characteristic hazards. Even more time must elapse during which large numbers of patients are followed and compared with patients on whom more familiar therapeutic procedures have been performed. At the present time, the surgical technique of pulmonary resection has been fairly well developed and standardized, but the observation of the results obtained through its use is still in its early phase. Until comparatively recently, indications for resections were based largely upon medical necessity. Patients came to the thoracic surgeon for resection because there simply was nothing else available for them. Any extensive use of the operation as an elective procedure was limited by the high morbidity and mortality rates which accompanied it. Table I contains statistics collected from the literature, reporting operations done previous to 1947 from three large surgical clinics. In a total of 343 operations, the morbidity rate was 51 per cent, the mortality rate 28 per cent.

TABLE I. COLLECTED STATISTICS

SURGEON	NUMBER OF PATIENTS	MORBIDITY		MORTALITY	
		NUMBER	PER CENT	NUMBER	PER CENT
Overholt[1]	200	82	41	51	25
Bailey[2]	80	56	70	23	27.5
Sweet[3]	63	36	57	21	33
Totals	343	174	51	95	28

Our experience previous to 1947 was quite similar. We had done 27 resections with a morbidity rate of 37 per cent and a mortality rate of 29 per cent.

THE HAZARDS OF PULMONARY RESECTION IN TUBERCULOSIS

The high morbidity and mortality rates previously described were not due to any fault in surgical technique, since the immediate operative mortality was extremely low, but were rather due to factors inherent in the disease itself. Since 1947, we have performed 96 resections on 95 patients, making a total of

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123 operations in 122 patients in the six-year period. The causes for the complications and deaths were not long in being recognized, and fall into three categories:

1. Progression of pulmonary disease
    - A. Early bronchopneumonia, either tuberculous, nontuberculous, or mixed.
    - B. Late. Evolution of latent or new foci of disease in the lung.
2. Opening of the bronchial stump
    - A. Early, due to failure to heal.
    - B. Late, due to progressive ulceration and sloughing.
3. Empyema
    - A. Early, due to overwhelming contamination at surgery.
    - B. Late, due to progression of pleural tuberculosis.

TABLE II. HAZARDS OF PULMONARY RESECTION FOR TUBERCULOSIS

PRIMARY COMPLICATIONS	TOTAL, 123 OPERATIONS				35 OPERATIONS NO STREPTOMYCIN*				88 OPERATIONS STREPTOMYCIN			
	MORBIDITY		MORTALITY		MORBIDITY		MORTALITY		MORBIDITY		MORTALITY	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Spread of Disease	11	9.0	7	5.7	7	20.0	6	17.1	4	4.5	1	1.1
Early	9		7		7		6		2		1	
Late	2		0		0		0		2		0	
Opening of Bronchial Stump	5	4.0	3	2.4	5	14.1	3	8.6	0		0	
Early	1		1		1		1		0		0	
Late	4		2		4		2		0		0	
Empyema	6	4.9	1	0.8	4	11.4	1	2.8	2	2.3	0	
Early	1		1		1		1		0		0	
Late	5		0		3		0		2		0	
Wound Infection	1	0.8	0		1	2.9	0		0		0	
Operative	2	1.6	2	1.6	0		0		2	2.3	2	2.3
Unknown	2	1.6	2	1.6	0		0		2	2.3	2	2.3
Total	27	22.0	15	12.2	17	51.5	10	28.6	10	11.4	5	5.7

*Included are 8 patients whose organisms had become streptomycin resistant due to long-continued heavy doses. All had serious complications.

In studying the complications which occurred in our patients, we have placed in one group those who did not receive streptomycin, or whose bacilli had become resistant to it through long continued large dosage; and in a second group all those patients who received effective streptomycin therapy.

A spread of their disease occurred in 7, or 20 per cent, of the 35 no-streptomycin patients, with a mortality of 6, or 17.1 per cent. This complication occurred in 4.5 per cent of the 88 patients who received streptomycin with a mortality of only 1, or 1.1 per cent.

Opening of the bronchial stump occurred in 5, or 14.1 per cent of the no-streptomycin group, with a mortality of 3, or 8.6 per cent. In the streptomycin group this complication did not occur.

TABLE IV. INDICATIONS FOR RESECTION IN TUBERCULOSIS

PRIMARY INDICATION	TOTAL: 123 OPERATIONS			NO STREPTOMYCIN: 35			STREPTOMYCIN: 88		
	NUMBER	MORBIDITY	MORTALITY	NUMBER	MORBIDITY	MORTALITY	NUMBER	MORBIDITY	MORTALITY
1. Collapse failure	25 = 20.3%	7 = 28. %	6 = 24. %	10 = 28. %	5 = 50. %	4 = 40. %	15 =17. %	2 = 13.2%	2 = 13.2%
2. Destroyed lung	10 = 8.1%	6 = 60. %	4 = 40. %	6 = 17.7%	4 = 67. %	3 = 50. %	4 = 4.5%	2 = 50. %	1 = 25. %
3. Chronic bronchial disease	51 = 41.5%	8 = 15.7%	5 = 9.8%	13 = 37. %	6 = 46. %	3 = 23. %	38 = 43. %	2 = 5.3%	2 = 5.3%
4. Diagnostic	5 = 4. %	0	0	1 = 3.2%	0	0	4 = 4.5%	0	0
5. Elective	32 = 26. %	6 = 18.7%	0	5 = 14.2%	2 = 40. %	0	27 = 31. %	4 = 14.8%	0
Total	123 = 100%	27 = 22. %	15 = 12.2%	35 = 100%	17 = 51.5%	10 = 28.6%	88 = 100%	10 = 11.4%	5 = 5.7%

of the smaller bronchi was suspected but not proved, are not included in this group, but comprise a rather large segment of the elective group—especially among the patients receiving lobectomy. It is in this third group that streptomycin has been most helpful in preventing complications and death. As will be seen in Table IV, the mortality rate among the patients in this group not receiving streptomycin was 23 per cent, whereas among the patients receiving streptomycin, it was only 5.3 per cent. Actually there were no tuberculous complications from it, the two deaths which did occur being operative deaths—one due to an unfortunate anesthetic complication, and the other due to unmanageable postoperative shock.

4. Diagnostic problems. Occasionally it is unwise to delay surgery while a time-consuming search is made by culture or animal inoculation for tubercle bacilli. This is especially true in the older age group of patients where bronchiogenic carcinoma may be suspected. It has been our policy to explore these patients, and if the diagnosis cannot be made by gross examination alone, or of an available lymph node, to resect the lobe in question. When the pathologic examination discloses carcinoma, the remainder of the lung is resected. There were 5 patients in this group with no postoperative complications.

5. Elective. This is the second largest group in our series. It includes all patients in whom a choice was made between resection and thoracoplasty, or some other surgical collapse procedure. About one-half of our lobectomies fall into this classification. As the indications for resection become better defined, it will probably become smaller. At present, the selection of patients for resection requires the combined wisdom of the medical and surgical team. It must be based upon a thorough knowledge of the patient's past reactions to his disease, an expert appraisal of his present status, and a wide experience in various forms of surgical therapy. It goes without saying that the patient must have had a prolonged period of observation under controlled conditions, and a thorough diagnostic work-up including the best in x-ray and bronchoscopic studies.

Among the considerations which have led us to do elective resections are the following:

A. Suspected, but not proved, tuberculous bronchial disease. It is becoming increasingly apparent that there is more tuberculous bronchitis than has been preoperatively diagnosed. Buckles and Neptune[6] have reported studies on 57 resected lungs. In 14 per cent, tuberculous bronchitis was diagnosed preoperatively, but it was found by the pathologists in 66.6 per cent. Likewise, Overholt and his co-workers[7] report in a study of 62 lungs resected after thoracoplasty failure, a pathologic finding of tuberculous bronchial disease in 64.5 per cent, as compared to a preoperative diagnosis in 37.1 per cent. Auerbach[8] found tuberculous bronchitis in 42.1 per cent of 1,000 consecutive autopsies on tuberculous patients. Jones and associates[9] conclude that bronchiectasis arises in reinfection disease in 50 per cent of fatal cases, and that it develops with surprisingly high incidence after primary tuberculosis in children. In our experience, patients whose disease remains more or less stationary, with no definite x-ray indication of cavity, yet a persistent or occasional positive sputum, are especially suspected of having tuberculous bronchial disease. The x-ray finding of "honey-combing" always leads us to suspect bronchiectasis. We believe that most such patients will not get well without a resection.

B. Patients whose past roentgenograms show a large amount of disease, which has partially healed with considerable scarring and fibrosis. Such lobes or lungs are likely to become the seat of much chronic pulmonary suppuration, even though adequately collapsed by thoracoplasty.

C. Cavities which have reopened after discontinuation of a therapeutically adequate pneumothorax are not likely to respond well to a second collapse procedure.

D. Cavities located near the hilum or mediastinum may either fail to respond to thoracoplasty, or require such an extensive one as to sacrifice a great deal of good lung tissue. In such cases, resection may prove to be the more conservative procedure.

E. Nonexpendable lung, frequently seen after long continued pneumothoraces, is often best treated by decortification of the "good" lobe, and a resection of the diseased one.

F. Tuberculomas of any considerable size, which have been under observation for some time without apparent change, should be considered for resection.

RESULTS

The immediate results in our series of 123 resections have been dealt with in considering the complications and indications (see Tables III and IV). We have not experienced a large number of late complications, such as reactivation, which others (notably Sweet[10]) have reported. We have continuously adhered to the principle that in resecting a lobe or a lung, we were merely removing the worst of the patient's tuberculosis, and thereby putting him in a favorable condition to control the remainder of the disease. We have insisted before accepting patients for resection, that they agree to undergo a prolonged period of bed rest following surgery. This practice we believe to be very important in preventing late complications.

Our patients have been referred to us from various physicians and sanatoriums, including many from out of the state. Follow-up studies, if they are

TABLE V. BARLOW SANATORIUM PATIENTS

	OPERATIVE RESULT			SPUTUM STUDIES			
OPERATION	NUMBER	MORBIDITY	MORTALITY	IMMEDIATE NEGATIVE	LATER NEGATIVE	TOTAL NEGATIVE	ALTERNATELY NEGATIVE AND POSITIVE
Lobectomy	15	2	0	11	2	13	2
Pneumonectomy	19	4	2	9	5	14	3
Total	34	6 (17.6%)	2 (5.9%)	20	7	27 (84.4%)	5

to be of any great significance, require that the patients be examined with similar techniques and under like conditions. Sanatoriums which have facilities for careful and extensive follow-up studies, are the most suitable sources for accumulating accurate information.

Among our patients are 34 from Barlow Sanatorium. Of these, 2 died in the hospital and did not return to the sanatorium (see Table V). Of the 32 who returned to the sanatorium, 20, or 62.5 per cent, had immediate and persistently negative sputum. By negative, we mean at least three consecutive pooled sputum and gastric washings injected into guinea pigs with negative results. An additional 7 patients converted to negative while in the sanatorium, making a total of 27, or 84.4 per cent, with persistently negative sputum. Five, or 15.6 per cent, had alternately positive and negative examinations, with the latest one negative in 4, and positive in one. In none of them has the sputum been continuously positive. Fifteen had surgery more than two years ago. Fourteen of these are working and in good health. One still has active disease in the contralateral lung. This disease was present at the time of surgery. In addition to the 2 patients who died, 4 patients developed complications following surgery. One had a bronchopleural fistula with empyema. She has closed the fistula and converted the sputum, and is awaiting additional surgery to eradicate the empyema. One had a pure tuberculous empyema appear a year after surgery. Sputum has remained persistently negative. One had a late appearance of disease in the remaining lobe after resection of the right upper and middle lobes. He has since had the pneumonectomy completed and has a negative sputum. One developed an ipsolateral spread, or reactivation, after segmental resection. She had two negative sputum and gastric examinations before the new disease appeared. She has since had a thoracoplasty with two negative examinations since the thoracoplasty.

It is interesting that one of the patients who died did well for five days and then developed x-ray evidence of contralateral disease. This disease continued to spread even though the patient was on streptomycin, and other antibacterial agents. He finally died sixteen days postoperatively, and the postmortem examination showed extensive disease in the contralateral lung. No tubercle bacilli could be cultured from the lung, and the microscopic slides were very puzzling to the pathologists. It was finally decided that the monocytic type of infiltration was most characteristic of a tuberculous reaction even though the picture was not entirely characteristic of that disease. It was classified as a death due to a tuberculous spread.

POSTRESECTION THORACOPLASTY

We feel that the question of the need for thoracoplasty following resection has not been entirely settled as yet. Early in our experience we performed few postresection thoracoplastics. Following receipt of reports from other clinics describing frequent reactivation in patients not protected with thoracoplasty, we have performed this operation routinely following pneumonectomies, and in selected cases following lobectomy. Yet a study of results in our earlier cases who did not receive thoracoplasty does not give convincing evidence of the need for it in any but selected cases.

TABLE VI. THORACOPLASTY VS. NONTHORACOPLASTY

	NUMBER	EARLY COMPLICATIONS	LATE COMPLICATIONS		TOTAL	
			TUBERCULOUS	NONTUBERCULOUS	NUMBER	PER CENT
No postresection thoracoplasty	61	3	3	3	9	14.7
Lobectomy	29	0	2	0	2	6.9
Pneumonectomy	32	3	1	3	7	21.9
Postresection thoractoplasty	35	4	0	0	4	11.5
Lobectomy	10	2	0	0	2	20.0
Pneumonectomy	25	2	0	0	2	8.0

As will be seen in Table VI, 29 lobectomies and 32 pneumonectomies did not receive postresection thoracoplasty in the immediate period following resection. Of this number, two lobectomies and three pneumonectomies later had thoracoplasty performed because of complications. Early complications arising in patients receiving thoracoplasty were about the same as in those not receiving thoracoplasties. No late complications have yet appeared among the 35 patients who received thoracoplasty. One late empyema developed among the 61 patients who did not receive thoracoplasty. One late ipsolateral spread occurred in a patient who had a middle and upper lobe resection without thoracoplasty (see Barlow Sanatorium report). Three patients developed a nontuberculous complication which required thoracoplasty for its correction. All three were right-sided pneumonectomies. Two of them had symptoms due to marked shift of the mediastinum, and one had right-sided heart failure. But thus far there have been no reactivations of disease in any of the pneumonectomy patients on whom we did not perform a thoracoplasty. Neuhof and Nabatoff[11] recently published results of angiographic study of the form and function of the remaining lung after pneumonectomy. They observed that whether mediastinal shift was great or little, the change in form and function of the remaining lung is not so great as we have been led to expect.

SUMMARY

1. A series of 123 consecutive pulmonary resections on 122 patients performed between 1944 and the end of 1949 has been studied. Among them are 34 carefully followed patients from Barlow Sanatorium who have shown a sputum conversion of 85 per cent.

2. The hazards of pulmonary resection for tuberculosis are chiefly the hazards inherent in the disease itself, rather than in the operative procedure. In our experience, they have been markedly reduced by the effective use of antibacterial agents, such as streptomycin. In 35 patients not receiving streptomycin the morbidity was 48.6 per cent and the mortality 28.6 per cent. In 88 patients receiving streptomycin the morbidity was 12.5 per cent and the mortality 5.7 per cent.

3. Primary indications for resection which we have observed have been: (1) collapse failure, (2) destroyed lung, (3) chronic bronchial disease, (4) diagnostic problems, and (5) elective. In the latter group are such indications as suspected, but not proved, bronchial disease; cavities poorly situated for response to thoracoplasty; cavities which have reopened after discontinuation of successful pnuemothorax; tuberculomas; and cases in which there is extensive fibrosis and scarring of pulmonary tissue due to tuberculous disease. We are of the opinion that chronic tuberculous bronchial disease in its various manifestations is by far the most important indication for resection.

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PULMONARY RESECTION FOR TUBERCULOSIS WITH STREPTOMYCIN

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ALTHOUGH one of the first planned lobectomies for pulmonary tuberculosis was done by Dr. S. O. Freedlander, in 1934, at Cleveland City Hospital, there had been little enthusiasm for pulmonary resection here until the advent of streptomycin. Fifteen cases of resection were done prior to the use of streptomycin. The first patient is still living, with a negative sputum. However, because of a 20 per cent operative mortality rate and many complications, other forms of therapy were used whenever possible. We wish to review fifty-three consecutive cases of pulmonary resection with streptomycin performed for tuberculosis between March, 1947, and August, 1949. These comprise the cases selected for pulmonary resection from the 800 beds at Lowman Pavilion and Sunny Acres Hospital, the sanatoriums serving the City of Cleveland and Cuyahoga County. In a combined conference the medical and surgical staffs of both institutions determine all therapy, and selected this group for resection. Forty-six pneumonectomies and seven lobectomies comprise the fifty-three cases in this series. There were four deaths, a mortality of 7.5 per cent. Each patient in this series received streptomycin before, during, and after surgery. Following surgery, a modified thoracoplasty, as suggested by Overholt and associates,[1] was carried out after pneumonectomy and upper lobectomy. A permanent phrenic interruption was done following lower lobectomies.

The main indications for resection were those commonly used: (1) destroyed lung, (2) bronchial stenosis, and (3) collapse failure. Some of the cases fell under more than one heading, but the principal indication was chosen for classification in this study.

In the selection of patients resection was considered to be a radical, irrevocable, and occasionally hazardous procedure. It was felt that, in comparison to other types of therapy, it should offer the only or the best chance of cure. It must be remembered that functioning pulmonary tissue as well as diseased tissue is usually removed by resection. Where pulmonary function is borderline, overenthusiasm for resection may result in a respiratory cripple or death. In our cases, resection has not been used when it was felt that lesser measures of therapy would reasonably control the disease. Unless there was an urgent or specific indication for resection, collapse procedures have been employed. On the other hand, when it was felt that a collapse measure such as thoracoplasty was of questionable value, or where the patient would ultimately remain with one functioning lung, resection was the primary choice. This was done in preference to the performance of a multiple stage thoracoplasty, with its attendant dangers of spread, and the possibility of a later

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resection which in our experience is usually more difficult than an initial resection. Chronic bronchial stenosis was considered an absolute indication for resection, other factors permitting. One group of patients in whom it was thought that resection offered the best chance for successful treatment were the cases of unilateral acute pneumonic tuberculosis.

Table I illustrates the indications for resection and lists the number of cases in each category.

TABLE I

INDICATION		NUMBER OF CASES
1. Destroyed lung		26
A. Extensive acute pneumonic disease	16	
B. Nonacute disease	10	
2. Bronchial stenosis		14
3. Collapse failure		10
4. Tuberculoma		2
5. Hemorrhage		1
Total number of cases		53

Observations can be made best from a study of the results and complications of each group separately.

DESTROYED LUNG

Of the fifty-three cases, twenty-six were resected for a destroyed lung. By destroyed lung is meant a condition in which the pulmonary tissue of one lung or lobe shows complete or almost complete involvement by cavitation, extensive pneumonic disease, chronic fibrocaseous disease, or by a combination of these. Of the twenty-six patients, sixteen had extensive acute unilateral disease. The remaining ten were operated upon for fibrocaseous disease with cavitation. The only lobectomy in this group was done for a giant cavity.

In the ten nonacute cases, there were nine pneumonectomies. Five were in colored and four in white patients. Seven were women and two were men. The youngest was 15, the oldest was 43, and the average age was 29.6 years (see Table II). There were no complications in this group, either during or after surgery; at present all are living and well from two years to eight months postoperatively. One patient in this group was treated by left lower lobectomy for a giant cavity. Postoperative course was uneventful except for a small acute spread to the left upper lobe almost immediately after resection. This was controlled by a permanent phrenic nerve operation and pneumoperitoneum. He is working full-time one and one-half years after operation.

TABLE II

DESTROYED LUNG—TEN CASES			
Pneumonectomies	9	Lobectomy	1
White	5	Male	3
Colored	5	Female	7
Age Range:— 15 to 43 years			
Average:— 29.6 years			
Complications:—Spread to remaining lobe in lobectomy			

The group of sixteen acute cases comprises the largest number of patients under one category. It also contains three of the four deaths. All sixteen patients required *pneumonectomy*, although one was done for technical reasons after a lobectomy had been successfully performed. There were thirteen colored and three white patients in this group, and of these, nine were men and seven women. The youngest was 19, and the oldest 54 years of age. The average age was 32 years.

Table III

ACUTE PNEUMONIC DISEASE—SIXTEEN CASES			
Pneumonectomy	16		
White	3	Male	9
Colored	13	Female	7
Age Range:—	19 to 54 years		
Average Age:—	32 years		
Complications:	Wound Infections		2
Deaths	(3-16)		18.7%

In reviewing these cases, other than the three deaths and two wound infections, there is a gratifying lack of incidents to report. All patients received streptomycin prior to surgery, varying from twenty-six to eighty days. The average was 46.6 days of streptomycin. The dosage was 1 Gm. per day. The patients were observed carefully while on streptomycin, and when it was felt that they had obtained their optimum result from this therapy, operation was performed. All the patients had been very febrile prior to the institution of streptomycin therapy. Two cases continued to have a low-grade fever at the time of surgery. The others had been afebrile from seven to 165 days, an average of forty-three days, before surgery. The operative procedure itself was easier than in the chronic cases. Adhesions were usually not present, or when present were thin, delicate, and easily dissected, unless there had been previous infection. The postoperative course was no different than that of the more chronic cases. The majority of the patients had a relatively afebrile course. It was noted that almost invariably, about one week after operation, their general appearance was improved and they had a feeling of well-being which was apparent even at this early date.

Of the sixteen acute patients, three died, a mortality of 18.7 per cent. Of the remaining thirteen patients, one was killed one year postoperatively following discharge from the hospital, when she was stabbed with a knife in the remaining lung. Twelve patients are living and well, from two and one-half years to six months postoperatively. It is interesting to note that while the mortality rate in the acute cases was 18.7 per cent, there was only one death in the thirty-seven nonacute patients, a mortality rate of 2.7 per cent. For this reason the three deaths in the acute group will be considered in some detail.

CASE REPORTS

The first death occurred in a Negro man, C. K., aged 23 years. The right upper lobe was the seat of dense, pneumonic disease with a four-centimeter cavity. The middle and lower lobes contained scattered disease. The dissection of the lung from the chest wall was difficult. At the end of the procedure, the blood pressure was 70/30, the patient having received 1,200 c.c. of saline, 500 c.c. of plasma, and 1,500 c.c. of whole blood. He received an additional 500 c.c. of plasma and 500 c.c. of blood during the afternoon and died five hours postoperatively of acute pulmonary edema. This patient's pulmonary edema was probably due to the injudicious use of intravenous fluids.

The second death was that of B. K., a white man, aged 51 years, who had a first-stage thoracoplasty on Nov. 27, 1948, under local anesthesia, for a large cavity at the right apex. Postoperatively he had a massive bronchiogenic spread to the entire right lung. Right pneumonectomy was performed on Jan. 26, 1949. The pleural cavity was contaminated by the rupture of a small caseating focus as the lung was being taken from the wound. The postoperative course was febrile, but not too stormy, until seven days postoperatively, when the patient suddenly went into mild shock with a temperature of 38.5° C. He complained of pain in the right upper quadrant of the abdomen, with tenderness and slight spasm.

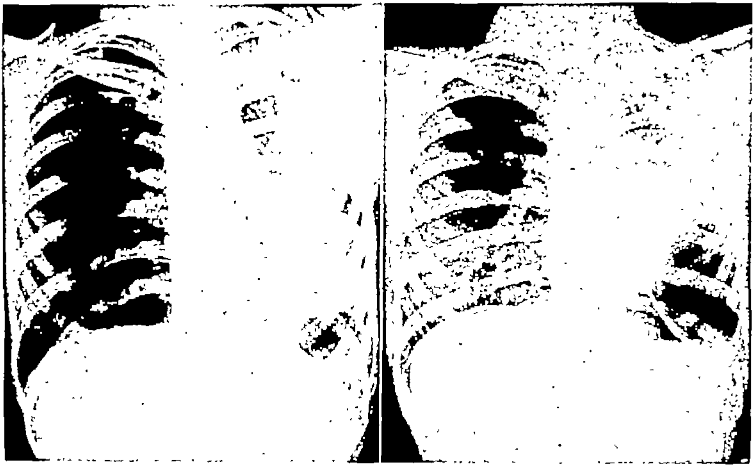
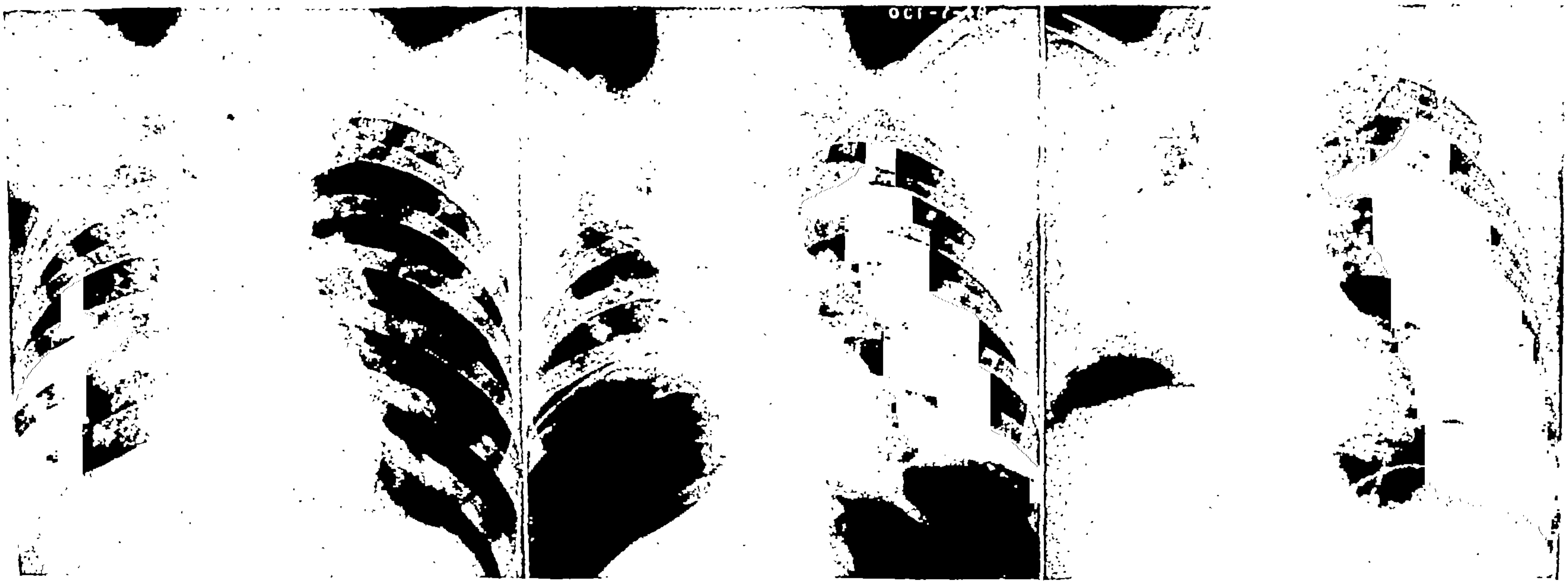

A. B.

Fig. 1.—A, Admission roentgenogram of the chest (March 6, 1947) on the first patient with acute disease which was resected. B, Preoperative roentgenogram (June 12, 1947) on the same patient.

Following this episode the patient developed cough and continued to run fever. The wound, which had been healed, broke down in small areas, about three weeks postoperatively. About the same time he started to raise sputum colored with old blood. A postpneumonectomy thoracoplasty was done in two stages, forty-six and forty-seven days after pneumonectomy. After this procedure the patient was in poor condition. He died seventy days after pneumonectomy with a bronchopleural-cutaneous fistula, infected wound, and spread to the contralateral lung.

The third death was that of J. F. R., a Negro man, aged 42 years. A diagnosis of pulmonary tuberculosis had been made in December, 1948. A roentgenogram of the chest revealed dense disease throughout the right upper lobe with considerable scattered disease in the middle and lower lobes. At operation, the apex of the lung was densely adherent and an apical cavity was opened in the dissection of the lung from the pleura. The pleural space was aspirated daily for two weeks after operation, with streptomycin and penicillin being instilled into the pleural cavity to prevent an empyema. The postoperative course was apparently uncomplicated when, on the twenty-fifth day after surgery, he had a sudden



A. *B.* *C.*

Fig. 2.—*A*, Admission roentgenogram of the chest (Oct. 2, 1947) on B. K., the second reported death. Cavitation is present. *B*, Prethoracoplasty roentgenogram on B. K. (Oct. 7, 1948). *C*, Postthoracoplasty roentgenogram on B. K. (Nov. 30, 1948) showing increase of disease at the right base which showed no change up to the time of pulmonectomy.

chill and elevation of temperature to 39.8° C., with a complaint of "soreness of abdominal muscles." The abdomen was diffusely tender. It was apparent that the patient had a bronchopleural fistula, and he began expectorating brown fluid. His course remained febrile in spite of therapy. Postpneumonectomy thoracoplasty was done on the forty-ninth postoperative day in an effort to obliterate the pleural space and to close the bronchopleural fistula. He quickly developed contralateral spread, remained febrile, and died eighty-three days following pneumonectomy.

In these two patients with bronchial fistulas, it was first thought than an empyoma developed as a result of the spill of purulent material which occurred at the time of surgery and that the bronchial fistulas were secondary to this. These cases were treated for two weeks after surgery by daily complete aspirations of fluid from the pleural cavity and the instillation of 1 Gm. of streptomycin and 500,000 units of penicillin. There was no evidence of infection in the pleural fluid which was aspirated daily.

There were seven cases of pleural contamination in the thirty-seven nonacute cases, which were treated similarly with no untoward developments. For this reason we think that the pleural contamination was not the cause of the fatal sequence of events. Despite the careful closure and pleuralization of the bronchus in each case a bronchial fistula developed for some unexplained reason in these two. Bronchoscopy before surgery and examination of the specimens postoperatively revealed no bronchial disease.

There is evidence in these cases that when a bronchial fistula does occur it is quickly followed by a severe reaction. The reaction may be a sudden change in intrapleural pressure or signs of irritation to the pleura as manifested in B. K. on the seventh postoperative day, by mild shock, a temperature of 38.5° C., pain, tenderness and slight spasm in the right upper quadrant of the abdomen, and the development of cough. In the case of J. F. R., after an uneventful course, the patient on the twenty-fifth postoperative day, suddenly developed a chill, temperature of 39.8° C., and soreness of the abdominal muscles. In the future, any such episode shall be considered as evidence of opening of the bronchus. The patient shall be taken to surgery and an eight-rib thoracoplasty will be carried out, during which time the pleural cavity will be evacuated, the bronchus inspected and resutured if necessary. This procedure would perhaps be unnecessary if the thoracoplasty were done at the time of pneumonectomy, as advocated by Iverson and Skinner.[3] We believe that the combination of the two procedures is ideal, especially in acute disease. However, after a brief experience this combination has been judged too extensive for most of our patients.

In a recent case of pneumonectomy for tuberculosis, not included in this report, mild shock occurred on the fourth postoperative day. A sensation of air bubbling in the chest was felt by the patient, there was sudden deviation of the trachea to the unoperated side, and air was aspirated from the pleural space where only fluid had been obtained previously. Two days later her temperature, which had been normal during the postoperative period, went to 38.5° C. The procedure as previously outlined was carried out. No bronchial fistula was found. Her subsequent course has been uneventful.

The first opening of the bronchus may be only small or temporary, because our patients did not cough up bloody fluid, or have other evidence of a sizeable permanent opening of the bronchus at the time of the first acute episode. It may be impossible or not feasible to close a bronchial fistula as has been suggested. In these two cases there was a time lag of twenty-one days and thirteen days from the first symptoms of bronchial opening until it was definitely known that a bronchial fistula existed. If the bronchus were inspected immediately the defect might be so small that successful repair could be accomplished. In any case a complete eight-rib thoracoplasty done before gross infection had set in should offer a better chance of healing than after extensive infection and drainage had been done. Antibiotics are also more effective early. The chances of thoracoplasty wound infection after gross infection of the pleural space are increased because of infection extending from the pleura through the pneumonectomy rib defect into the soft tissues of the chest wall.

BRONCHIAL STENOSIS

Fourteen patients had bronchial stenosis. Eight had stenosis of the mainstem bronchus and six of an upper lobe bronchus. In all the diagnosis was made preoperatively by bronchoscopy and was the primary indication for resection. Lobectomy was planned in four of the cases with upper lobe bronchial stenosis. However, at operation a significant amount of disease was found in the lower lobe, and it was felt that it was dangerous to allow this to remain. Therefore, pneumonectomy was done in these cases.

Of these patients thirteen were female and one male. Three were colored and eleven white. The youngest was 26, the oldest 57, and the average age was 34.4 years (see Table IV). In all cases the bronchial stenosis and pulmonary disease were mainly chronic in type. It was noted at operation that the bronchus was difficult to dissect, due to a peribronchial inflammatory reaction which was more marked than in any other group. There were no complications during or after surgery, with the exception of one wound dehiscence. The wound was resutured and healed without infection. All patients in this group are living and well, sputum negative, from two years and ten months to eight months after surgery.

COLLAPSE FAILURE

Ten patients were operated upon for collapse failure. Only five were reported to have bronchial stenosis by pathologic examination of the specimens. Five were failures of thoracoplasty to close the cavity. Three had been treated

TABLE IV

BRONCHIAL STENOSIS—FOURTEEN CASES			
	Pneumonectomy	14 Cases	
White	11	Female	13
Colored	3	Male	1
	Age Range:—	26 to 57 years	
	Average Age:—	34.4 years	
	Complications:	None	

with pneumothorax, pneumoperitoneum and phrenic crush, and two were failures of pneumothorax alone. There were six pneumonectomies and four lobectomies in this group.

TABLE V

COLLAPSE FAILURES—TEN CASES			
Pneumonectomies	6	Lobectomies	4
Collapse Used:			
Thoracoplasty	5	Pneumothorax	2
Pneumothorax, Phrenic Crush and Pneumoperitoneum			3

These patients all had a fair trial of one or more of the collapse procedures. The shortest period of collapse was six months in a patient treated by thoracoplasty. The longest was thirty-six months (a combination of pneumothorax, phrenic crush, and pneumoperitoneum). The average duration of collapse was nineteen months. One of the patients was colored and nine were white. The youngest was 22 years of age, the oldest 48, and the average age was 31.5 years (see Table VI). The resections following thoracoplasty were technically more difficult than the average. One of the cases was complicated preoperatively by an effusion positive for tubercle bacilli, and infected thoracoscopy sinus tracts.

There were three tuberculous wound infections in this group, and one death. Two of the wound infections were excised at the time of thoracoplasty and healed per primum. The third occurred in the case that died. Death was due primarily to respiratory insufficiency in one of the lobectomies. One patient was living and well for two years, sputum negative, and with no sign of activity of the disease. She died suddenly at home one night before she could be seen by a physician. An autopsy was not obtained. One has recently developed a cavity in the remaining lung one year after resection. One died seventeen months after surgery of cor pulmonale; the remaining six cases are living and well, sputum negative, from thirty to ten months postoperatively.

TABLE VI

COLLAPSE FAILURES—TEN CASES			
White	9	Female	7
Colored	1	Male	3
Age Range:—	22 to 48 years		
Average Age:—	31.5 years		
Complications:	Wound infections		3
	Deaths		1

TUBERCULOMA

There were two cases which were interpreted as tuberculoma. Both cases had positive sputum and other signs that the lesion had developed caseation. Both were female, one colored and one white. Each was treated by lobectomy and both had uneventful postoperative courses. They are both living and well, sputum negative, eight and eleven months after resection.

HEMORRHAGE

One case was done for hemoptysis. The patient was a 28-year-old Negro man for whom a thoracoplasty had been planned and the first stage carried out. Several days later, severe hemoptysis occurred and pneumonectomy was performed as a life-saving procedure. Pathologic examination of the lung revealed erosion of the cavity into an adjacent blood vessel. The patient also had an extensive caseous pleurisy which was decorticated. The postoperative course was stormy, but without major complication. He has had no pulmonary spread of the disease seventeen months after surgery, but he did develop tuberculous osteomyelitis of the left foot and ankle, for which an amputation was done in September, 1949.

SUMMARY

Fifty-three consecutive cases of pulmonary resection for tuberculosis are presented. Four deaths occurred, a surgical mortality of 7.5 per cent. There were three deaths in the sixteen acute cases, a mortality of 18.7 per cent. All of the patients received streptomycin before, during, and after surgery. Of the forty-nine patients who survived, none developed complications such as bronchopleural fistula or empyema, and only one has developed a spread on the contralateral side. Although the mortality was higher in the patients with acute pneumonic disease, it is felt that in these cases especially, resection offers almost the only chance of recovery. Observation in the patients who developed bronchopleural fistulas has led us to the conclusion that the opening of the bronchus may be small at first, and may be characterized by mild shock, upper abdominal pain, and fever. It is our belief that the results of this complication may possibly be prevented by immediate thoracoplasty with inspection and resuturing of the bronchus, if possible. To date, the results of pulmonary resection with streptomycin have been impressive. We feel that this procedure is now an important part of our armamentarium in the treatment of patients with pulmonary tuberculosis.

The authors are indebted to Dr. Sidney E. Wolpaw for advice rendered during the preparation of this paper.

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PRIMARY NEUROFIBROSARCOMA OF THE DIAPHRAGM

Report of Two Cases

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THE unique character of primary diaphragmatic tumors is intriguing to both the clinician and the pathologist because of the combined problem of diagnosis, therapy, and cell derivation.

While several different cell types have been encountered, a search of the literature fails to reveal any primary tumor of the diaphragm classified as neurofibrosarcoma. It seems worth while, therefore, to record two personal cases, believed to be the first so reported.

INCIDENCE OF PRIMARY DIAPHRAGMATIC TUMORS

Scott and Morton[1] collected thirty-three primary tumors of the diaphragm which had been reported between 1868 and 1946. Four of these were not established by operation or autopsy and have been discarded. This leaves a total of twenty-nine proved cases. Since 1945, Rosenthal and Frissell,[2] Van Alstyne,[3] Branwood and Glazebrook,[4] and Grow, Bradford, and Mahon[5] have contributed four additional tumors. The two cases of the present report increase the total to thirty-five. Seventeen of the thirty-five tumors were classified as benign and eighteen as malignant.

The cell types were recorded as follows:

Table I

BENIGN		MALIGNANT	
Lipoma[6-9]	4	Fibrosarcoma[2, 20-24]	6
Cyst[1, 10, 11]	3	Rhabdomyosarcoma[25, 26, 27]	3
Fibroma[12, 13]	2	Myosarcoma[28]	1
Chondroma[14]	1	Leiomyosarcoma[27]	1
Angiofibroma[15]	1	Fibromyosarcoma[29]	1
Hemangioendothelioma[3]	1	Round-cell sarcoma[30]	1
Lymphangioma[16]	1	Undifferentiated sarcoma[31]	1
Neurofibroma[17]	1	Mixed cell sarcoma[4]	1
Rhabdomyofibroma[18]	1	Hepatoma from embryonic cell rest[32]	1
Fibromyoma[19]	1	Neurofibrosarcoma (present report)	2
Fibroangioendothelioma[5]	1		
Total	17	Total	18

Surgical excision was performed in fourteen cases. While there is a paucity of information regarding postoperative survival times, the results which have been reported are given in Table II.

CASE REPORTS

Case 1.—H. Y., a 56-year-old white man, was referred to us* in February, 1946. In 1940, the patient was admitted to the Alameda County Hospital with the complaints of swelling of the right ankle and knee, and fleeting pains with stiffness in the joints of the right wrist,

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*By Dr. Kenneth Jenkins.

TABLE II

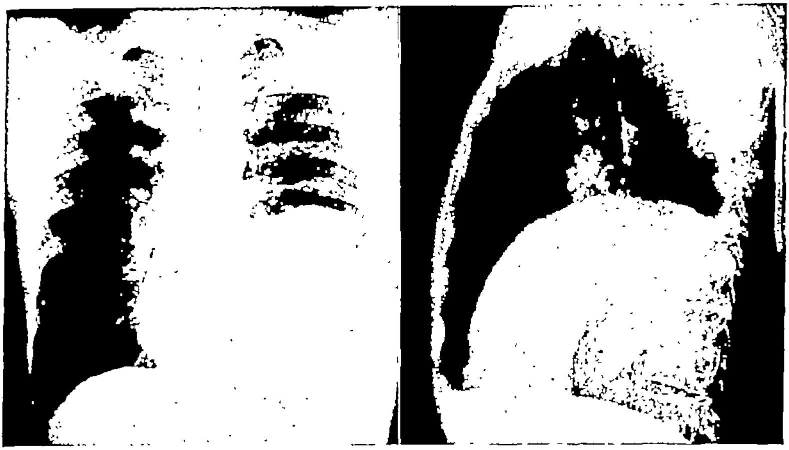
AUTHOR	DATE	TYPE	SIDE	RESULT
Primary Benign Tumors				
1. Bonamy[13]	1912	Multiple fibromas	Right	Recovery
2. Soderlund[6]	1937	Lipoma	Left	Recovery
3. Kinsella[10]	1939	Fibromyoma	Right	Recovery
4. Butler[10]	1939	Cyst	Left	Recovery
5. Arkless[18]	1942	Rhabdomyofibroma	Left	Recovery, died 7 years postop. from causes other than tumor
6. Soto[7]	1943	Lipoma	Right	Recovery
7. Robson and Collis[11]	1944	Cyst	Right	Recovery
8. Klassen, Patton, and Bemen[17]	1945	Neurofibroma	Right	Recovery, well 7 months postop.
9. Scott and Morton[1]	1946	Cyst	Left	Recovery
Primary Malignant Tumors				
1. Gross[20]	1911	Fibrosarcoma	Left	Recovery, died 7 months postop. from recurrence
2. Sauerbruch[20]	1913	Fibromyosarcoma	Left	Recovery
3. Gale and Edwards[32]	1939	Hepatoma (embryonic cell rest)	Right	Recovery, well 7 months postop.
4. Ackermann[21]	1942	Fibrosarcoma	Right	Recovery
5. Samson and Childress (Case 1)	1946	Neurofibrosarcoma	Left	Recovery, well 4 years postop.

fingers, and toes. Roentgenograms of the hands and feet at that time were normal. The joint symptoms had subsided somewhat during the four-year period from 1941 to 1945. In 1946, only careful questioning revealed symptoms referable to the chest. The patient had had a chronic cough for many years which had become more pronounced during the previous year. For possibly one year the patient admitted to mild dyspnea on exertion which he had completely ignored and, on bending forward, a sense of fullness and weight in the left chest. The cough had not been productive and there was no blood spitting, wheezing, or pain in the chest.

Physical examination showed a thin, sallow-complexioned man appearing older than the stated age. Distinct clubbing of the fingers was present which, the patient said, had been called to his attention three years previously by members of the family. The left lower chest showed slight limitation or motion. There was dullness posteriorly from the seventh rib downward which was not changed by deep inspiration. The right lung was normal. The heart sounds were normal and the blood pressure was 130/80. The liver and spleen were not palpable. Details of the roentgenographic findings are given in Figs. 1 and 2.

The only abnormal laboratory finding was a coagulation time of eighten minutes. Vitamin K was given prior to surgery. The left lower chest was aspirated and no fluid was obtained. The needle encountered firm resistance. Among other intrathoracic lesions, a diaphragmatic tumor was considered.

Left posterior thoracotomy was performed on March 14, 1946. Through a curved incision, the eighth rib and a posterior segment of the seventh rib were removed. The pleural cavity was opened exposing a large nodular tumor occupying the entire left lower pleural cavity. The tumor was firm and had a poorly developed capsule. Many large veins, almost sinuses, coursed over the surface of the tumor. These passed through numerous firm adhesions attached posteriorly to the parietal pleura and superiorly to the diaphragmatic surface of the left lower lobe. There was no adherence to the pericardium. The left lower lobe and lingula were atelectatic from pressure. The diaphragmatic surface of the lower lobe was separated from the tumor by sharp dissection. This resulted in considerable oozing and leakage of air. Numerous suture ligatures were necessary to obliterate the large venous sinuses and prevent a massive hemorrhage from the surface of the tumor. After separating all adhesions the tumor was partially delivered through the incision and the inferior surface inspected. The base was concave and arose from the central tendinous portion of the diaphragm. The superficial layer of the tendinous portion was peeled away with the tumor leav-



A. *B.*

Fig. 1, *A* and *B* (Case 1).—Roentgenogram, frontal and lateral projections. The mediastinum and heart are not displaced. The density at the left base has a rounded upper border. Fluoroscopically, this border descended slightly on deep inspiration. Films made with the Potter-Bucky grid showed no evidence of bony erosion.

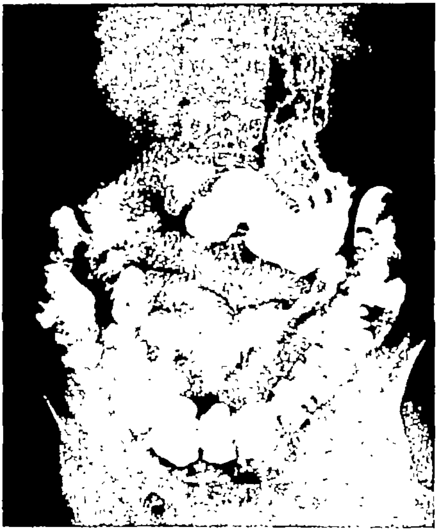


Fig. 2 (Case 1).—A simultaneous barium study of the stomach and colon shows no evidence of displacement or of pressure defects. This was believed to rule out both eventration of the diaphragm and an infradiaphragmatic mass.

ing several small perforations into the peritoneal cavity. The diaphragm was opened and its inferior surface inspected. There was no evidence of neoplastic extension. The diaphragm was then closed in two layers with interrupted silk. The torn surface of the lung was repaired and the lower lobe brought to full expansion under positive pressure. The pleural cavity was not drained. During and immediately following surgery a total of 2,000 c.c. of whole blood and 500 c.c. of plasma were given. The patient left the operating room in excellent condition.

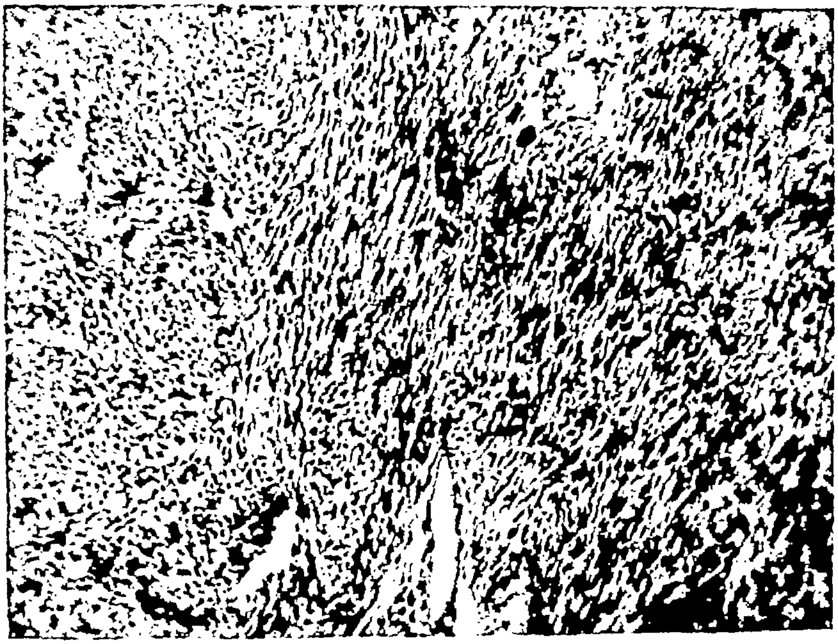


Fig. 3 (Case 1).—Photomicrograph ×100. There is characteristic palisading with neurogenous elements intermixed with fibroblasts. There is round cell infiltration showing some inflammatory change.

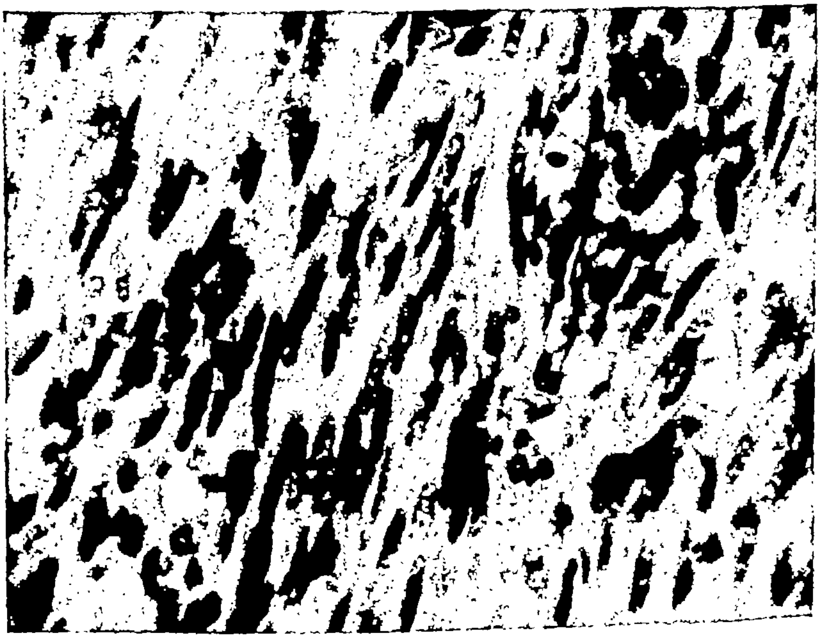


Fig. 4 (Case 1).—Photomicrograph ×500. The elongated and fusiform-shaped spindle cells with numerous mitotic figures are characteristic of metaplasia into true sarcoma.

Postoperatively, there occurred a transient atelectasis of the left lower lobe. Several aspirations of fluid from the pleural cavity were necessary. The patient was discharged home on the twelfth postoperative day.

The tumor was roughly ovoid, measuring 20.5 by 15.0 by 10.0 cm. and weighing 1,755 grams. The upper end was slightly pointed and the lower surface was flat measuring 12.5 by 10.0 cm. The tumor was firm and surrounded by a fibrous capsule measuring from 3 to 6 mm. in thickness, except near the flattened surface where the capsule broadened to a depth of 3 cm. In this portion of the capsule was an isolated nodule measuring 3 by 2 by 2 cm. which was slightly softer than the remainder of the tumor mass. The cut surface showed interlacing bands of white and pinkish-white tissue. One small cystic area was demonstrated. Microscopic examination* showed a fibrous and neural stroma with scattered areas of necrosis and degeneration. In some areas, there was metaplasia of the fibrous elements into true sarcoma. In these regions the cells were hyperchromatic, spindle-shaped, and moderately pleomorphic with fairly frequent mitotic figures (Figs. 3 and 4). The small soft nodule described previousy was composed almost completely of this type of cell.

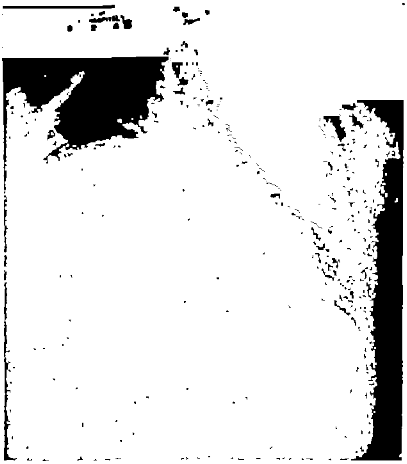


Fig. 5 (Case 2).—Roentgenogram, frontal projection with Lipiodol filling. There is a large density obscuring over one-half of the right lung field. The upper border is rounded. On the original film no endobronchial obstruction was seen. Atelectasis of the right middle and right lower lobes was suggested. (No other films were suitable for reproduction.)

The patient convalesced slowly but progressively from operation. During the nine succeeding months he gained at least fifteen pounds. The clubbing of the fingers gradually receded, with return to normal in approximately six months. Almost from the day of operation he completely and permanently lost all stiffness and pain in the smaller joints. Four years following surgery the patient was working steadily. He had a morning cough productive of a slight amount of mucopurulent sputum. Thorough physical and roentgenographic examinations showed no evidence of recurrence of the tumor.

Case 2.—E. L., a 50-year-old white housewife, was admitted to the San Joaquin General Hospital in September, 1946, because of increasing dyspnea over a period of six months. In March, 1946, she had been placed on digitalis therapy. One month later she noted ankle edema, more pronounced in the afternoon. During the month prior to admission she lost twenty pounds and suffered from anorexia, constipation, increasing weakness, and fatigability. On September 4, a dull aching pain appeared in the right upper abdomen and right shoulder. This pain was accentuated by deep breathing. There was no hemoptysis or cough.

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*By Dr. Gertrude Moore.

Physical examination revealed a markedly obese female who was orthopneic. The temperature was 101.6° F., the pulse 100 per minute, and the respirations 32. There was an inspiratory lag of the right hemithorax and absent breath sounds with dullness to percussion over the lower one-half posteriorly. The abdomen was pendulous and palpation in the right upper quadrant provoked pain. A one plus pitting edema of the ankles and pretibial areas was present. No clubbing of the digits was noted.

The erythrocyte count was 4,100,000, the hemoglobin was 11 Gm., and the leucocyte count was 12,000. The Kline serologic test was negative, and the urine revealed a one plus albumin. Circulation time by the Decholin method was eight seconds and by the ether method seven seconds.

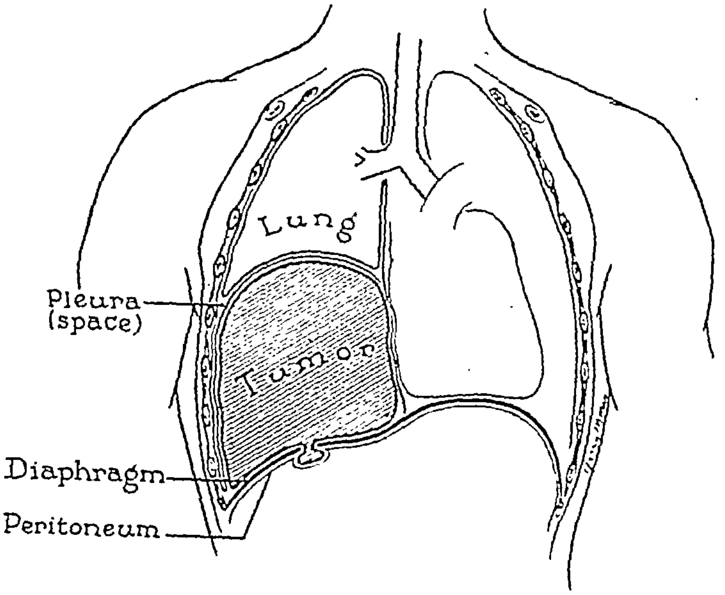

Fig. 6 (Case 2).—Schematic drawing of the situation seen at post-mortem examination. The tumor is entirely extrapleural and has pushed the heart to the left. The pedicle has pierced the diaphragm forming a 2 cm. tumor nodule lying extraperitoneally below the diaphragm.

Details of the roentgen films are shown in Fig. 5. Fluoroscopic study indicated that the mass moved synchronously with the right hemidiaphragm. Films following the induction of a pneumoperitoneum disclosed the mass to be supradiaphragmatic. Bronchograms showed no evidence of intrabronchial disease, although atelectasis of the right lower lobe was suggested.

Three attempts at right thoracentesis failed to obtain any free fluid. Bronchoscopy disclosed a horizontal take-off of the right-stem bronchus with an upward swerve of its distal portion. There was moderate narrowing of the lumen throughout.

It was felt that the patient had an extrapulmonary mass originating in the right lower hemithorax, and a diaphragmatic tumor was considered. Exploratory thoracotomy was advised but the patient died suddenly before surgical intervention was undertaken. No single cause of death was discovered, although the patient's sudden death was not surprising in view of the decreased pulmonary function, poor cardic reserve, and obesity.

At autopsy there was complete atelectasis of the right lower lobe and partial collapse of the middle and upper lobes. A tumor measuring 23 by 22 by 11.5 cm. and weighing approximately 3,000 grams completely filled the right lower hemithorax up to the level of the sixth rib posteriorly. When viewed alone it appeared to be a perfect mold of the space it occupied with intermittent grooves for the ribs. The inferior surface was concave and attached by a ½ cm. pedicle which pierced the hemidiaphragm through its tendinous portion and expanded into a tumor nodule 2 cm. in diameter below (Fig. 6). The tumor was entirely extrapleural and extraperitoneal. The inferior mediastinum was pushed to the left and was connected to the tumor by dense fibrous tissue which contained numerous large veins. There were no venous connections with the lung. The growth was firm and on cut sections revealed scattered areas of xanthochromia.

The histologic picture* presented the same cellular elements as found in Case 1 (Fig. 7).

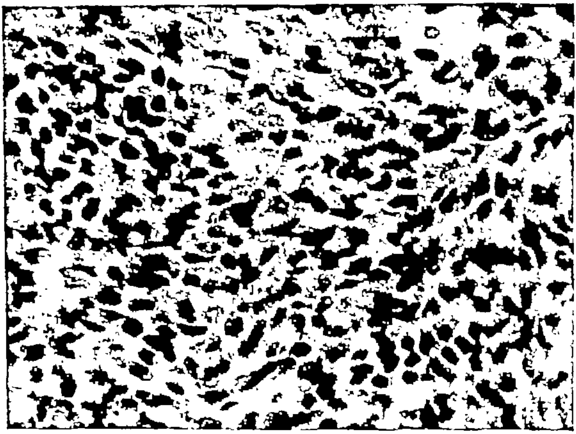

Fig. 7 (Case 2).—Photomicrograph ×500. The neurogenous elements are evident. There is extensive pleomorphism of the cells with some attempt at palisading. There is obvious malignant degeneration and mitotic figures are numerous.

COMMENT

Of particular interest was the effect of surgery on the joint symptoms and clubbing of the fingers in Case 1. Van Hazel[33] discussed joint manifestations in a group of seven patients with intrathoracic tumors and cited two in whom the joint symptoms abruptly disappeared following operation. Klassen's[17] patient showed no clubbing but suffered from arthralgia and joint-swelling in the hands and feet. These symptoms disappeared following operation. More recently, Berg[34] reported six additional cases in which dramatic improvement from arthralgia and clubbing of the digits followed removal of intrathoracic tumors. Of the nine cases thus collected, three were benign tumors of the mediastinum, one was a benign tumor of the diaphragm, one was a benign tumor of the lung, and four were primary carcinomas of the lung.

It is recognized that the majority of patients with intrathoracic tumors do not manifest hypertrophic pulmonary osteoarthropathy. This discrepancy is due to unknown or unrecognized factors. Van Hazel and others believe there is evidence that chronic anoxemia may be an important factor in the development of clubbing. He postulated that the anoxemia may be due to neoplastic involvement of, or direct pressure on, hilar pulmonary vessels, particularly the veins. A comparison of the findings in our two patients suggests, however, that neither the pressure hypothesis nor anoxemia per se can fully explain the occurrence of joint manifestations. The first patient showed no clinical signs of anoxemia, although the original complaints of arthralgia antedated the discovery of the tumor by nearly six years. The second patient was obviously anoxemic. She had orthopnea. The tumor was larger and extended higher in the hemithorax. There was more extensive atelectasis and obviously greater pressure on the pulmonary hilum, particularly the inferior pulmonary vein, yet joint symptoms failed to become manifest. It is not inconceivable that this tumor grew rapidly and that the patient died before sufficient time had elapsed for the development of arthralgia or clubbing.

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*Described by Dr. Paul Michael.

Another possible factor bearing on the development of joint manifestations concerns the blood circulation. While both tumors described previously were exceptionally vascular, there was one important difference in venous drainage. In Case 2 (without arthralgia) the venous return was mainly into the mediastinum, thus the venous blood of the tumor emptied into that of the greater circulation. In Case 1 (with arthralgia) large venous sinusoids connected the tumor with the pulmonary circulation as well as with the parietes. Thus, the main volume of reduced hemoglobin from the tumor probably emptied into the oxygenated blood of the pulmonary venous circulation. This condition may well have had the same circulatory effect as an intrapulmonary arteriovenous fistula. Patients with the latter lesion also frequently exhibit clubbing of the digits.

Fried[35] has expressed the opinion that hypertrophic pulmonary osteoarthropathy is not unlike acromegaly. He has observed the former condition in patients with bronchiogenic carcinoma; then demonstrated hyperplasia of the eosinophilic cells of the anterior hypophysis at necropsy. Fried thus suggests that the motivating disorder is dispituitarism which is provoked by disease of the lungs.

DISCUSSION

Tumors of the diaphragm have now progressed from an academic to a practical category. They are uncommon but important from a therapeutic standpoint. In keeping with the contemporary medical dictum of "constant awareness," we emphasize that at one stage malignant diaphragmatic tumors are amenable to surgical excision. They remain only to be diagnosed during the docile interval.

The signs and symptoms are governed by the size and location of the tumor on the diaphragmatic surface. As a rule, they do not appear until the lesion has attained considerable magnitude. Dyspnea, cough, and thoracic discomfort may result from pressure atelectasis. Other symptoms less commonly encountered have been gastrointestinal upsets, shoulder pain, effusions, and hemoptysis. The work load of the heart may be increased by a large excessively vascular tumor, in effect, the introduction of a new circulatory system. In patients whose cardiac reserve is otherwise limited (such as in Case 2), this additional factor may well lead to cardiac decompensation and exitus.

Roentgenograms and fluoroscopy will aid in localization and in study of the pathologic dynamics of the mass. If there is roentgen evidence of a tumor adjacent to eroded vertebrae, thought should be given to intraspinal Pantopaque studies to rule out intrathoracic meningocele.[36] An anomalous lobe of an otherwise normal liver[37] may roentgenographically mimic a diaphragmatic tumor. It may be impossible, however, to delineate between a supra- and infradiaphragmatic position without utilizing pneumoperitoneum.

When a tumor occupies the supradiaphragmatic position, it should be identified as extra- or intrapulmonary. Bronchoscopic exploration eliminates visible endobronchial extensions of an intrapulmonary tumor and affords opportunity for the cytologic study of bronchial secretions. Bronchographic mapping may reveal distortion of the tracheobronchial tree due to extrinsic pressure. If distortion is present and there is no endobronchial pathology, an extrapulmonary tumor is strongly suggested. Pneumothorax may be instituted but the roentgenographic interpretation should be cautious. A tumor attached to an atelectatic pulmonary base may present a homogeneous shadow which makes the differentiation between intra- and extrapulmonary positions difficult. If the pneumothorax is adequate thoracoscopic inspection may be considered but, in general, both pneumothorax and thoracoscopy are discarded procedures in such a situation.

In the final analysis, exploratory thoracotomy always should be undertaken both for diagnosis and for treatment unless the operative risk is prohibitive.

SUMMARY

1. Two cases of primary neurofibrosarcoma of the diaphragm are described. No other tumor of this particular cell type involving the diaphragm has been found in the literature.

2. In both patients, diaphragmatic tumor was considered in the differential diagnosis. The first patient has remained well for four years following surgical removal; the second patient died suddenly before exploration could be carried out.

3. Thirty-three additional examples of primary tumor of the diaphragm have been collected from the literature. Of this total of thirty-five, seventeen were considered to be benign and eighteen malignant.

4. The relationship of arthralgia and clubbing of the digits to intrathoracic tumors is discussed.

5. Diagnostic approaches to diaphragmatic tumors are enumerated.

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THE COMPLICATIONS OF STELLATE AND THORACIC SYMPATHETIC NERVE BLOCKS

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STELLATE GANGLION BLOCK

DENERVATION of the stellate ganglion and the thoracic sympathetic ganglia by block with local anesthetic drugs is a common practice in the diagnosis and therapy of an increasing number of diseases and injuries. It is inevitable that some undesirable complications result from the widespread utilization of the procedures. It is the purpose here to outline in some detail the nature of these complications and the factors responsible for their development. The need for a realistic appraisal of the potentialities for harm in completing stellate ganglion and thoracic sympathetic blocks is apparent on anatomic grounds alone. There is a constant proximity of important structures which cannot be invaded by the exploring needle with impunity.

Anatomy.—The anatomy of the stellate ganglion must be reviewed briefly. A bilateral structure, it originates from the fusion of the first thoracic sympathetic ganglion and the inferior cervical ganglion to form a semilunar mass approximately 2.5 cm. in length and 0.5 cm. wide in the majority of specimens. This general configuration is fairly constant although the actual shapes of the ganglia vary widely. Posteriorly, the stellate ganglia lie on the lateral surface of the first thoracic and seventh cervical vertebrae between the head of the first rib and the vertebral artery at its junction with the subclavian. The carotid sheath containing the carotid artery, jugular vein, and vagus nerve lies anteriorly and slightly lateral. The phrenic nerve, lying in the scalenus anticus muscle is lateral and the bodies of the first thoracic and seventh cervical vertebrae are medial. The sympathetic chain and the ganglion lie on the deep fascia which covers the anterior surface of the longus capitus, longus colli, and scalenus anticus muscles.

The stellate ganglion is illustrated in Fig. 1 to point out the mechanism of the most important and serious complications of nerve block in this region. Particular reference is made to the apex of the lung immediately lateral to the stellate ganglion and the exposed intervertebral foramina of the cervical spine which offer an avenue to subarachnoid injection of local anesthetic drugs.

The position of the apex of the lung makes it entirely feasible to induce pneumothorax if the advancing needle is somewhat off its course. It is interesting although possibly unnecessary to point out, that induction of a pneumothorax by allowing air to leak in between the layers of pleura from the external environment is not very easy to accomplish in the scarred apical position of the adult lung. It appears more likely that the pneumothorax is the consequence of

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pulmonary perforation with an air leak from the lung to the pleura. The belated awareness of symptoms and the occasional instance of tension pneumothorax support this concept. Another point of practical importance is the actual height of the apex of the lung. Ordinarily, the apex of the lung is considered to be level with the first rib posteriorly or 4 cm. above the clavicle anteriorly. Simple observation and some thought will indicate that these guides are approximations at best. The apex of the lung is mobile when it is not adherent to the chest wall and moves *down* with inspiration, a point of some importance if the phase of respiration is to be employed as assistance in minimizing the danger of pneumothorax. The apex of the lung also varies in position with disease and body habitus. These are anatomic factors which should be remembered in performing stellate ganglion block.

The mechanism of subarachnoid anesthesia as a complication of stellate block is more easily understood. The dura may be perforated in an intervertebral foramen or in areas where its extension peripherally about a somatic nerve makes it peculiarily liable to injury and perforation.

The presence of other structures shown in the diagram suggests further possible complications. However, none of these, except for intravascular injections, has proved important or serious in executing stellate block.

Techniques.—The techniques of stellate block, as described in the literature, are varied and large in number.

The classic technique is that introduced in this country by Labat as modified by White.[1] This has since been largely replaced by many anterolateral, lateral, or anterior approaches making use of Chassaignac's tubercle or the cricoid cartilage as landmarks.

In the anterolateral approach used by Volpitto and Risteen[2] a wheal is raised 2 cm. inferior to Chassaignac's tubercle and 1 cm. above the midclavicular point. An 8 cm. needle is introduced downward and medially at a 45° angle with the sagittal plane of the body to encounter the transverse process of the seventh cervical vertebra or the first rib at a depth of 5 to 6 cm. The needle is withdrawn and the angle changed to 80 to 90°. It is then advanced to 6 to 8 cm. where it should encounter the body of the first thoracic vertebra. This approach has been varied by individuals with a radius of 3 to 4 cm. for the skin wheal. Still other variations involve encountering Chassaignac's tubercle first and then redirecting the needle toward the seventh cervical vertebral body.

Murphey[3] described another "anterior approach" with a puncture site at the lateral edge of the scalenus anticus muscle at the level of the cricoid cartilage. A spinal needle is directed with the point posteriorly at an angle of 5 to 15° with the horizontal. The needle, passing behind the carotid sheath and superior to the apex of the lung, impinges on the stellate ganglion or the body of the seventh cervical vertebra.

Fitspatrick and Higdon[4] described the simple technique in which the skin wheal is made over Chassaignac's tubercle. The needle is inserted directly toward the tubercle and is then redirected slightly anteriorly and inferiorly to the body of the seventh cervical vertebra.

Ochsner and DeBakey[5] prefer a modification of Leriche's technique. Using a skin wheal 1 cm. medial to the upper border of the midpoint of the clavicle, a needle is *inserted* at a 45° angle 6 to 7 cm. between the vertebral and carotid arteries. They have also described an approach lateral to the vertebral arteries.[6]

Findley and Patzer[7] described an anterior or paratracheal approach. The skin wheal is made two fingerbreadths above the sternoclavicular junction just medial to the carotid artery. The needle is inserted straight down to the transverse process of the seventh cervical vertebra and then after withdrawing 2 mm. the injection is made.

The apparently endless varieties of methods which have been reported for completing stellate ganglion block have been successful in producing sympathetic paralysis. The important aspect of selecting a technique, in view of the ease in obtaining effective blockade, is the method which is least encumbered by untoward sequelae. Many of the excellent reports available are concerned exclusively with therapeutic effect or deal with such small numbers that no reasonable delineation of the complications is possible.

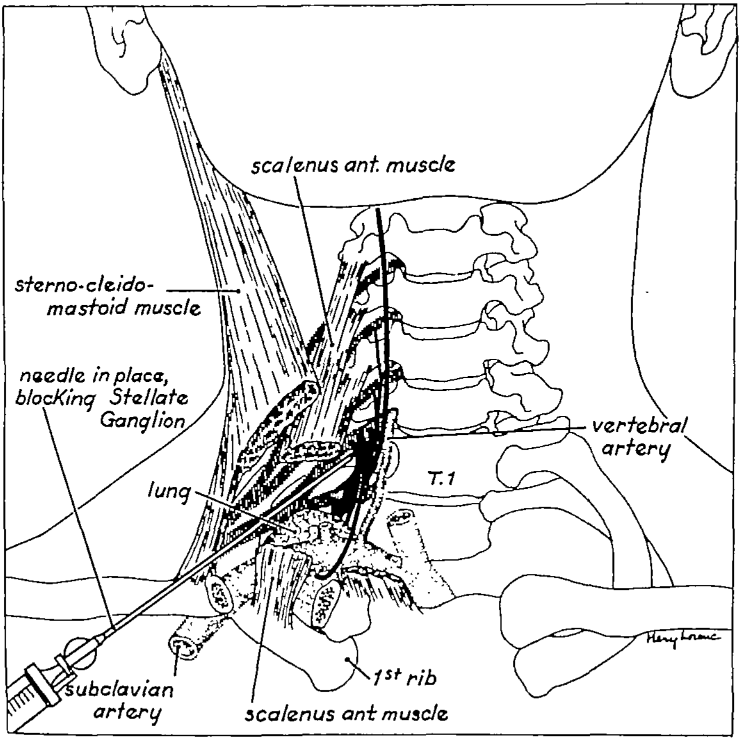

Fig. 1.—Diagrammatic representation of important structures associated with stellate ganglion block.

To ascertain the influence of technique upon the incidence and the nature of complications, an unselected series of 186 consecutive stellate ganglion blocks was studied (Table I). Blocks were performed by visiting and resident staff in a hospital caring for indigent patients only. The major complications with reference to the influence of technique are summarized in Table II. Although

TABLE I

DISEASE	NUMBER OF BLOCKS	NUMBER OF PATIENTS	CLINICAL RESULTS		
			GOOD	FAIR	POOR
1. Peripheral vascular disease	54	27	16	1	10
2. Asthma	69	41	25	7	9
3. Postmastectomy edema	4	2	1	1	0
4. Causalgic states	33	16	8	3	5
5. Angina	5	4	0	3	1
6. Cerebral accidents	10	10	1	4	5
7. Phantom pain	2	2	0	1	1
8. Carcinoma, tongue	2	1	0	1	0
9. Herpes zoster	1	1	1	0	0
10. Volkmann's contracture	3	1	1	0	0
11. Retinal artery thrombosis	1	1	0	1	0
12. Hyperhidrosis	2	1	1	0	0
Total	186	107	54	22	31

TABLE II. COMPLICATIONS OF STELLATE BLOCK

TECHNIQUE	NUMBER OF PATIENTS	NUMBER OF BLOCKS	SPINAL TAP (NO ANESTHESIA)	SPINAL ANESTHESIA	PNEUMOTHORAX	ACUTE ASTHMA	TOTAL INCIDENCE (PER CENT)
Posterior	8	8	0	1	1	0	25
Anterolateral	86	151	2	3	3	1	6
Anterior	13	27	0	0	0	0	0

the total numbers in each group are not strictly comparable, the paratracheal approach appears to be safest from the standpoint of serious complications.

Summary of Stellate Ganglion Blocks.—In the series studied, 186 stellate blocks were performed on 107 patients for the conditions and with prognostic, diagnostic, or therapeutic results as shown in Table I. Patients received from 1 to 5 blocks each, depending upon the clinical results obtained. Fourteen patients received bilateral blocks simultaneously and 16 patients received a block on the opposite side at an interval of at least twenty-four hours after the first block. The various techniques employed and their complications are shown in Table II. A transient aphonia or dysphonia noted in 3 of 27 blocks by the paratracheal approach is not included as a major complication. Alcohol was utilized in 37 of the 107 patients. Only 4 injections were judged unsuccessful, a high therapeutic efficiency regardless of technique.

The complications will be described in detail.

Complications

CASE 1.—The patient was a hypertensive 40-year-old woman who suffered repeated attacks of status asthmaticus uncontrolled by the usual medications. Five cubic centimeters of procaine were injected into both stellate ganglia using the anterolateral approach without incident. One month later, the same procedure was repeated with the same technique. Unfortunately, accidental subarachnoid injection resulted following which she was in profound shock for thirty minutes. Therapy with oxygen and vasopressors was successful. Four months after the accidental spinal anesthesia, an alcohol block of the right stellate ganglion was completed with no untoward effect.

Diagnosis.—Accidental spinal anesthesia.

CASE 2.—The patient was a 34-year-old man whose therapy for traumatic causalgia of the upper extremity was a series of stellate ganglion blocks. During the fourth block, by the anterolateral technique, he complained of dyspnea, vertigo, and then rapidly lost consciousness. He was given artificial respiration with oxygen for twenty minutes. Blood pressure, which was 80/60, was supported by ephedrine sulfate intravenously. It was interesting that during the time of respiratory paralysis the patient could thrust his legs about. After apparent recovery, the patient was allowed to go home that evening. He returned the next day because of headache. This was followed in a few days by pneumonia which cleared with antibiotic therapy.

Diagnosis.—Accidental spinal anesthesia.

CASE 3.—A 50-year-old woman with phantom pain, following amputation of the right upper extremity, had a stellate block by the posterior approach with 8 c.c. of 2 per cent procaine. At the end of the injection, there was frank respiratory difficulty. Sensory anesthesia was noted to the fifth cervical spinal cord level on the right and the fifth thoracic spinal cord level on the left. Motor paralysis was present in the right lower and the left upper extremities. The blood pressure was 80/50. She was treated with ephedrine and oxygen. Recovery was intact except for severe headache. The phantom pain was relieved and a Horner's syndrome persisted.

Diagnosis.—Accidental spinal anesthesia.

CASE 4.—A 30-year-old woman with old rheumatic heart disease and auricular fibrillation had embolization to the left brachial artery resulting in pain, reduced skin temperature, and palsy of the left hand and forearm. A left stellate block by the anterolateral approach was performed using 18 c.c. of 1.5 per cent procaine. Five minutes after the injection, the patient suddenly became agitated and apprehensive. Respirations gradually ceased in another minute. Unconsciousness ensued, the limbs became flaccid, the pupils were widely dilated. Artificial respiration with a Kreiselman bellows resuscitator[8] was immediately instituted. Color remained good. The blood pressure, five minutes after artificial respiration was begun, was 75/50 with a pulse of 60 per minute. Twenty-five minutes after the block, the patient was put in a Drinker respirator and nasotracheal intubation was performed. Ten minutes later the patient was able to move head and eyes but spontaneous respiration was inadequate for proper ventilation. Two hours and twenty-five minutes after the block, the patient was conscious and moderately alert. At this time she did not react on the endotracheal tube but indicated that it annoyed her. The respirator was stopped and spontaneous respirations were resumed. The endotracheal tube was removed. After the patient was taken from the respirator, she complained of pain in the left arm. Flexion of the fingers, previously impossible, was executed with little difficulty. The surface temperature of the affected hand was unimproved for the next twenty-four hours, at which time it gradually increased. Forty-eight hours after the block the temperature of the hand was normal and the brachial artery could be palpated at its distal third. Eight days later the radial pulse was first noted. Recovery was uneventful.

Diagnosis.—Accidental spinal anesthesia.

CASE 5.—A 30-year-old woman with intractable asthma had a right stellate block by the anterolateral approach with 4 c.c. of 1.5 per cent procaine. After the injection, readjustment of the needle was attempted and a spinal tap was done. Except for headache, recovery was uneventful.

Diagnosis.—Accidental spinal puncture.

CASE 6.—A 51-year-old man with asthma had a right stellate block by the anterolateral approach. Insertion of the needle yielded spinal fluid. The needle was withdrawn 0.5 cm. and blood aspirated. The needle was then withdrawn another 0.5 cm. and 4 c.c. of 2 per cent procaine injected. The patient returned in a week for a left stellate block with alcohol. The patient's condition was improved.

Diagnosis.—Accidental spinal puncture.

CASE 7.—A 40-year-old man with asthma had an acute asthmatic episode immediately following the injection of the stellate ganglion with 6 c.c. of 1.5 per cent procaine followed by 2 c.c. of absolute alcohol. This was treated unsuccessfully with epinephrine. Aminophyllin intravenously terminated the attack.

Diagnosis.—Acute asthma.

CASE 8.—A right stellate ganglion block was attempted on a 31-year-old asthmatic man by the anterolateral approach. No confirmatory signs of sympathetic paralysis were noted. Radiographic chest studies revealed an asymptomatic complete pneumothorax the next day. Recovery and expansion of the lung were uneventful.

Diagnosis.—Traumatic pneumothorax.

CASE 9.—A right stellate ganglion block by the posterior approach with 15 c.c. of 1.5 per cent procaine was completed upon an elderly woman with chronic asthma. The patient became very pale and experienced difficulty in breathing, resembling an asthmatic attack, almost immediately. No Horner's syndrome was presented. X-ray examination revealed a 50 per cent collapse of the right lung.

Diagnosis.—Traumatic pneumothorax.

CASE 10.—A middle-aged woman with status asthmaticus for two weeks was treated with a right stellate ganglion block by the anterolateral approach with 15 c.c. of 1.5 per cent procaine. Evidence of Horner's syndrome developed in five minutes. Ten minutes later increasing dyspnea and cyanosis were noted. Thoracentesis yielded over 1,000 c.c. of air.

Diagnosis.—Traumatic pneumothorax.

CASE 11.—A 26-year-old woman with bronchiectasis of the right middle, right lower, and left lower lobes was hospitalized because of increasing dyspnea. A right pneumonectomy was performed when bronchospirometry showed almost no ventilation in the right lung. Three months later a left stellate block using an anterolateral approach was performed because of chronic intractable asthma. A Horner's syndrome developed almost immediately without relief of the asthma. Four hours later the patient became acutely dyspneic and suffered circulatory collapse. The *diagnosis of tension pneumothorax* was confirmed at once and air withdrawn from the left pleural space. The expansion of the lung was maintained by continuous suction for four days. Recovery from the pneumothorax was satisfactory. The asthma was not controlled.

Diagnosis.—Traumatic pneumothorax.

THORACIC SYMPATHETIC BLOCKS

Anatomy.—The sympathetic trunk enters the thorax in front of the neck of the first rib, medial to the superior intercostal artery and the first thoracic nerve and posterior to the apex of the pleura. It descends anteriorly to the neck of the second rib, heads of the next three ribs, on the ligament radiatum for the next three, and finally on the sides of the lower thoracic vertebrae. Thus, the trunk gradually progresses downward, medially and anteriorly. It lies behind the pleura in its entire course.

Usually there are twelve sympathetic paired ganglia but their number may be reduced by the fusion of one or more ganglia. They send gray rami posteriorly and laterally to the intercostal nerves and receive white rami.

The cervical sympathetic trunk sends fibers to supply the structures of the head and neck. The stellate ganglion and the first through the fourth thoracic ganglia are accepted as the supply to the arm; the heart and aorta are innervated by the first through the fifth thoracic ganglia. The greater splanchnic nerves arise from the fifth to ninth thoracic ganglia to supply the aorta and esophagus and send fibers to the stomach, gall bladder, liver, and pancreas. The lesser splanchnic nerves from the tenth and eleventh thoracic ganglia supply the celiac ganglion and the least splanchnic from the twelfth thoracic ganglia goes to the renal plexus.

Techniques.—

The variations in techniques in thoracic sympathetic block are few when compared to those described for the stellate ganglion. Practically all are modifications of one of the techniques described by Labat[9] differing only slightly in angle and depth of the insertion of the needle.

Labat technique: The patient lies on the opposite side to the one to be injected in the posture commonly described for the induction of spinal anesthesia. The twelfth thoracic vertebra and the spinous process of the seventh cervical vertebra are used as landmarks. Wheals are raised opposite the appropriate spinous process 4 to 5 cm. from the midline. An 8 cm. needle is directed at a 25° angle with the saggital plane passing between the ribs and transverse processes until it impinges on the body of the vertebrae just in front of the intervertebral foramen. Three to 5 c.c. of procaine or 3 c.c. of alcohol can be used for anesthesia.

White[10] used 10 cm. needles and inserted them until the rib or transverse process was contacted at a depth of 2 to 5 cm. A rubber marker was then placed 3 to 4 cm. from the skin, the needle withdrawn to subcutaneous level, and reinserted at an angle of 30 to 25° to the medial sagittal plane and perpendicular to the curvature of the back in relation to the long axis of the thorax. Contact was made at the marker and injection was completed with 2 c.c. of 1 per cent procaine followed in five to ten minutes by 5 c.c. of absolute alcohol.

Seldon,[11] in performing the technique of Labat, preferred pentothal or other general anesthesia prior to the injection of absolute alcohol rather than risk dilution of the alcohol with procaine.

The group of patients reported here were blocked by a modified Labat technique. The patients are placed in a prone position with their arms hanging over the sides of the table. A pillow is then placed under the anterior surface of the body to exaggerate the curvature of the spine. Skin wheals are raised 4 to 5 cm. from the midline opposite the appropriate spinous process and 10 cm., 24-gauge, short beveled, stiletted needles are then inserted toward the midline at an angle of 20 to 30° with the sagittal plane at right angles with the vertical axis. If the rib or transverse process is not encountered, then the needle should impinge on vertebral body at a depth of about 8 cm. If the rib or transverse process is encountered, then the needle is withdrawn to subcutaneous depth and reintroduced cephalad at an angle of approximately 30°. The needles are so directed that they will be placed on the lateral part of the vertebral body. After all the needles are placed, the stilets are withdrawn and a drop of procaine placed on each hub. Aspiration into the needle indicates that the needle is within the pleural space and readjustment is necessary. If spinal fluid or blood emerges, misplacement of the needle is obvious. The syringe is attached after all tests are negative and 3 to 4 c.c. of 1.5 per cent procaine are injected. Paresthesias and/or anesthesia are not looked for; signs of sympathetic paralysis are used as the indication of correct placement of the needles. After ten minutes, 3 to 4 c.c. of absolute alcohol are injected through each needle. Patients are usually well sedated with an opiate and a barbiturate and general anesthesia is not required. The patient remains in the hospital only long enough to recover from the sedation and until evidence of stability of the cardiovascular system is established.

Combined cervicothoracic blocks are accomplished in two fashions. The first is a combination of a posterior stellate ganglion block with appropriate thoracic segmental block. The first skin wheal is placed opposite the spinous process of the seventh cervical vertebra and the needle inserted so as to impinge on the body of the seventh cervical or first thoracic vertebrae. This technique is useful for those conditions in which alcohol is to be used for stellate and thoracic sympathetic blockade. The second technique, fashioned after Pereira,[12] depends upon the gravity diffusion of procaine caudad with the patient in the semirecumbent position. Here a stellate block is performed by a paratracheal or anterolateral approach and if, after a small test dose, a Horner's syndrome is produced, then 20 c.c. of 1.5 per cent procaine are injected. Warming of the hand and arm indicates paralysis to the first and second and sometimes third thoracic vertebrae, as well as stellate paralysis. This is a useful technique, because of its relative simplicity and ease of performance, to use for therapy or diagnostic or prognostic block where the hand is involved. It has not been used with alcohol.

PARAVERTEBRAL THORACIC SYMPATHETIC BLOCK

Results.—Forty-two thoracic sympathetic ganglia blocks were performed on 36 patients for the conditions shown in Table III. Alcohol was used in 29 of the 36 cases (80 per cent). In 8 (27 per cent) cases of the 29 an alcohol neuritis developed. One patient developed a bleb of the skin following therapy to be described later. Complications occurred in 25 per cent of the patients treated. All blocks were successfully performed as judged by sympathetic paralysis with the exception of one patient who would not tolerate completion. This is listed as a poor result in Table III. Clinical cure did not parallel adequate denervation.

TABLE III. THORACIC SYMPATHETIC BLOCKS

DISEASES	NUMBER OF BLOCKS	NUMBER OF PATIENTS	RESULTS		
			GOOD	*FAIR*	*POOR*
Angina	28	24	16	3	5
Aneurysm (chest pain)	8	7	6	0	1
Dyspnea and hypertension	1	1	0	0	1
Herpes Zoster	1	1	1	0	0
Thrombophlebitis (arm)	1	1	1	0	0
Postmastectomy pain	2	1	1	0	0
Undiagnosed chest pain	1	1	1	0	0
Total	42	36	26	3	7

There were many occasions when a combination of stellate ganglia and thoracic sympathetic block was indicated. The experience of the combined procedure is summarized briefly in Table IV.

THORACOCERVICAL SYMPATHETIC BLOCKS

Results.—One hundred thirty thoracocervical sympathetic blocks were performed on 75 patients with the results shown in Table IV. Seventeen of the patients had complications which are listed in Table V. Alcohol was used in 50 patients, 4 of whom (8 per cent) developed annoying alcohol neuritis. One asthma patient died seven hours after the block but she was moribund when the block was performed. It was felt by all observers that the attempted therapy did not hasten the exitus. One other patient died with a pneumothorax.

The complications will be described in detail.

Complications

CASE 12.—A 51-year-old man with anginal syndrome underwent a prognostic block of the sympathetic ganglia of the first through the fifth thoracic ganglia with 1.5 per cent procaine 5 c.c. each. Upon exercise no anginal pain was elicited. Three days later the patient had the second through the fifth thoracic ganglia blocked with procaine followed by alcohol (4 c.c. each). Pain relief was excellent but the patient returned in eight days with alcohol neuritis of the segments blocked. Palliative treatment was advised and instituted with good results.

Diagnosis.—Alcohol neuritis.

TABLE IV. CERVICOTHORACIC SYMPATHETIC BLOCKS (COMBINED)

DISEASES	NUMBER OF BLOCKS	NUMBER OF PATIENTS	RESULTS GOOD	FAIR	POOR
Angina	52	24	14	8	2
Asthma	32	27	8	7	12
Axillary artery spasm	1	1	1	0	0
Thrombophlebitis	3	2	2	0	0
Buerger's disease	1	1	1	0	0
Raynaud's disease	8	5	4	0	1
Frostbite	5	2	1	0	1
Bronchiogenic carcinoma with metastasis	4	2	1	1	0
Causalgia	11	6	0	5	1
Phantom pain	2	2	0	2	0
Hyperhidrosis	5	1	1	0	0
Scleroderma	3	1	1	0	0
Volkmann's contracture	3	1	0	0	1
Total	130	75	34	23	18

TABLE V. COMPLICATIONS (COMBINED CERVICOTHORACIC SYMPATHETIC BLOCK)

Alcohol neuritis	4	
Anesthesia, left ulnar, T_1 and T_2	1	
Asthmatic attack	3	
Pneumothorax	4	(1 death)
Cord penetration	1	
Hemopneumothorax	1	
Aphonia	1	
Untoward drug reaction	2	
Total	17	(23 per cent of patients; 13 per cent of blocks)

Discussion.—In the 12 (15 per cent) cases of neuritis encountered of 79 cases in which alcohol was used, the onset ranged from one to twenty-three days with practically all in the six- to eight-day period. The neuritis lasted about one to two weeks in the majority of cases. Treatment varied, depending upon the severity of the symptoms, from mild analgesics to repeated procaine blocks of the sensory nerves. Usually only one or two blocks were necessary to keep the patient comfortable.

Alcoholic neuritis is the most common complication mentioned in this form of therapy. Various figures are found in the literature ranging from 0 to 90 per cent for the incidence of neuritis, but White and Smithwick[13] found that troublesome intercostal neuritis will be found in about 10 per cent of the patients. The incidence will be reduced if the needles are placed accurately on the lateral surface of the body of the vertebra anterior to the somatic nerves. If sympathetic paralysis without sensory paralysis follows the injection of 1 to 2 c.c. of procaine, then it is probable that neuritis will not follow the injection of 3 to 4 c.c. of alcohol.

CASE 13.—A 52-year-old man with a five-year history of severe bronchial asthma was being treated with a combined posterior stellate ganglion and second and third thoracic ganglia sympathetic block with procaine. The patient suddenly became dyspneic, apprehensive, and slightly cyanotic. There were signs and symptoms of traumatic pneumothorax present. He was treated with oxygen and positive pressure and the pleural space aspirated. He was removed to the ward where water-seal drainage was instituted and the patient placed in an oxygen tent. Forty-eight hours later the needle was removed from the chest. Following one more aspiration, the patient made an uneventful recovery.

Diagnosis.—Traumatic pneumothorax.

CASE 14.—A 35-year-old woman with severe bronchial asthma was admitted for thoracic sympathectomy. An "emergency block" was requested and the right stellate and the second and third thoracic sympathetics were blocked with procaine. The patient continued to breathe with severe embarrassment. After three to five minutes, she complained of auditory and visual disturbances. The pulse became slow at this point. She had a moderate convulsive attack and shortly thereafter respiratory efforts ceased. No pulse or heartbeat was felt. Endotracheal intubation and artificial respiration with oxygen had already been started. Epinephrine was injected directly into the heart and air was aspirated from the chest, but the patient did not recover. A post-mortem chest film showed a right pneumothorax.

Diagnosis.—Traumatic pneumothorax.

Discussion.—Pneumothorax is the most common of the major complications following thoracic sympathetic block. In 4 cases of 130 thoracic blocks, 1 ended fatally before therapy could be instituted. The pertinent anatomy of the thorax makes this a real danger. Surprisingly few instances of pneumothorax are reported in the literature but the possibility should always be considered.

CASE 15.—A 27-year-old man whose upper extremity was encased in plaster for forty hours as therapy for a fractured radius and ulna developed a Volkmann's contracture. A left stellate block was performed at once. The block was repeated two days later. Four days later it was felt that cervicothoracic sympathetic block would be more effective. The sympathetics of the first, second, and third thoracic ganglia were injected with 1.5 per cent procaine. The patient complained of pain in the chest immediately following the block but examination failed to show any pneumothorax. However, the next day dyspnea and tachycardia were evident. An x-ray examination showed a fluid level to the eighth thoracic vertebra and complete collapse of the left lung. Aspiration of the chest yielded 1,500 c.c. of blood. Some air was allowed to remain in the chest and a transfusion of 500 c.c. whole blood was given. After a stormy course, the patient recovered but the left upper lobe remained collapsed until a decortication was done.

Diagnosis.—Traumatic hemopneumothorax.

Discussion.—This is an unusual course of events not previously reported. It was believed that in the collapse of the lung small veins at the apex between the visceral and parietal pleura were torn resulting in hemorrhage.

CASE 16.—A 55-year-old man with a four-year history of bronchial asthma had a block of the right stellate ganglion and the sympathetics of the second and third thoracic ganglia with procaine and absolute alcohol. A Horner's syndrome developed immediately following the block but was absent eighteen hours later. The patient was not relieved of the asthma. One month later the patient returned for a left stellate block which was done with procaine, 1.5 per cent. No alcohol was injected because the block immediately precipitated a severe attack of asthma lasting fifteen minutes. Since the patient was practically free of attacks with adrenalin in oil, no further therapy was attempted.

Diagnosis.—Acute asthma.

Discussion.—The three asthmatic attacks precipitated by this form of therapy make it obligatory to perform all blocks with procaine before permanent sympatholysis is attempted with alcohol or surgery. The mechanism, rationale, and results of sympatholysis in patients with asthma has been reviewed by Miscall and Rovenstine.[14]

CASE 17.—A 43-year-old woman with syphilitic aortic aneurysm and the anginal syndrome first came to the clinic in November, 1939. She had a left stellate ganglion block with 5 c.c. of 1.5 per cent procaine and 1 c.c. of absolute alcohol. Attacks were less frequent and less severe. Two weeks later the procedure was repeated and six days later the second to the fifth thoracic sympathetic ganglia on the left side were blocked with procaine and absolute alcohol. The pain was relieved and the patient returned to the clinic in October, 1940 (one year later) for a repetition of the procedure. Ten months later, in June, 1941, she was blocked successfully again. In May, 1942, the patient returned with anginal pain and the left stellate and upper thoracic sympathetic ganglia were blocked with absolute alcohol. Five days later the patient was free of pain but exhibited anesthesia of the ulnar nerve and the first and second thoracic segments.

Discussion.—This case presents many interesting points. Anesthesia of a segment about the nipple is more frequent than is reported since many patients and physicians do not consider "the frozen area" important. The anesthesia carries little consequence if it does not involve the upper limb. It probably arises from the destruction of the sensory fibers by the alcohol and is related to the neuritis which occurs with incomplete destruction.

The regeneration of nerve fibers is well illustrated here. It is difficult to promise a patient more than six months to one year relief since sympathetic fibers can regenerate.[15]

CASE 18.—A 32-year-old man who developed hyperhidrosis totalis six months following a skull fracture was treated with right stellate ganglion block as a preliminary procedure. Two days later, while a left stellate ganglion block was being attempted, the dura was pierced and severe pain ensued. Anesthesia was noted on the left down to the umbilicus though no procaine was injected. The next day no residual anesthesia was noted and the patient went on to have the right stellate and second and third thoracic ganglia injected with procaine and alcohol.

Diagnosis.—Spinal cord penetration.

Discussion.—No serious consequences ensued from this case, but Molitch and Wilson[10] reported a vivid description of Brown-Séquard paralysis following therapy for angina pectoris.

CASE 19.—A 60-year-old man with angina pectoris had a block of the second to the fifth thoracic ganglia with procaine and absolute alcohol which gave relief of substernal but not precordial pain. He returned in two weeks with a history of a blister of three days' duration. This was located on the left side of the back about 6 cm. from the midline and over the fifth to the ninth ribs. There was hypoalgesia of the second to the ninth thoracic ganglia. Aspiration revealed a clear amber fluid.

Diagnosis.—Skin bleb.

Discussion.—Whether this is related to the block, skin preparation, or hypoalgesia cannot be said. *Nothing like it has been reported to our knowledge.*

CASE 20.—A 54-year-old man with angina pectoris having a diagnostic left stellate ganglion block developed severe bradycardia and cyanosis following the skin wheal and the introduction of the needle while in a sitting position. This cleared upon being placed in the prone position.

Diagnosis.—Drug reaction.

CASE 21.—A 44-year-old man with asthma had jerky convulsive movements with cyanosis following attempted procaine injection of the first, second, and third thoracic ganglia.

Diagnosis.—Drug reaction.

Discussion.—Whether these are true allergic reactions rather than psychosomatic affairs is difficult to say. Procaine reactions have been adequately described, but both these patients had subsequent uneventful thoracic sympathetic blocks with procaine and alcohol.

Comment.—Several striking features have become evident as a result of this survey of stellate ganglion and upper thoracic sympathetic blocks. Regardless of the technique utilized, successful denervation with procaine is easily attained. The therapeutic results in so far as patient care is concerned depend more upon intelligent choice of stellate or thoracic sympathetic block and less upon the technical skill of the anesthetist. This statement is obviously not pertinent in those instances where diagnosis or prognosis was the goal. In general, it appeared that blocks performed posteriorly or from the lateral aspect carried a higher potentiality of risk than those performed anteriorly. The major complications are pneumothorax and spinal anesthesia, although others have been observed. These are most important since they are most common and potentially fatal.

SUMMARY

1. The experience gained in 358 nerve blocks of the stellate and upper thoracic sympathetic ganglia upon 218 patients is presented.

2. Successful denervation is easily accomplished but at a risk of significant undesirable sequelae (5.9 per cent of the number of blocks).

3. Brief descriptions of 21 cases are employed to document the nature of the complications.

4. Traumatic pneumothorax, accidental spinal anesthesia, and alcohol neuritis are the most common untoward events.

5. The incidence of these complications is higher in posterior or lateral approaches to the sympathetic chain. The safest method for the cervical sympathetic is a *paratracheal* technique when possible.

6. Stellate ganglion and thoracic sympathetic block should be employed without hesitancy when properly indicated. However, since the procedures are not without considerable danger, adequate precautions must be observed to minimize the development of the complications noted in this study.

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CILIATED EPITHELIAL CYST OF THE ESOPHAGUS

Report of a Case

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Ciliated epithelial cysts of the mediastinum have been reported with increasing frequency within recent years and several reviews have described their clinical and pathologic features.[1,2,3,4] The occurrence of these lesions in the esophageal wall, however, is relatively uncommon. The cysts are congenital and generally thought to arise from a bud or diverticulum of the primitive foregut. Other theories assume the imperfect closure of a tracheoesophageal fistula or the isolation of one of the vacuoles normally present in the embryonic esophagus. Ranstrom[5] collected twenty such cases reported prior to 1946, and described two from his clinic. The majority of these patients were newborn

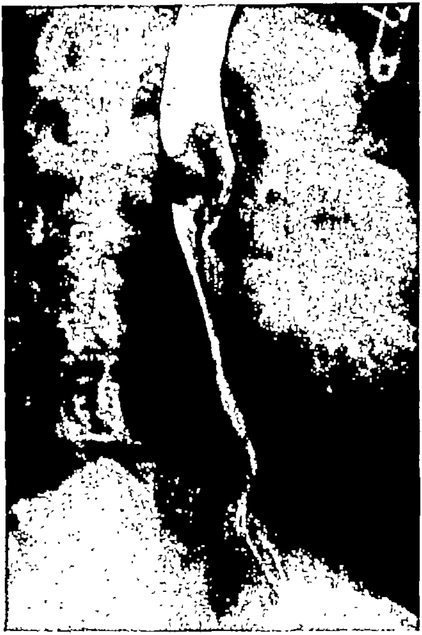

Fig. 1.—Preoperative film of esophagus with barium. A mass arises from the right lateral wall of the esophagus.

From the Tumor Service, United States Marine Hospital.

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infants in whom the diagnosis was made at autopsy. We have found but two cases in which ciliated epithelial cysts of the esophagus were removed surgically.[3, 6]

We have recently treated a young woman who presented the clinical features of a benign tumor of the esophagus. Pathologic study of the mass excised from the esophageal wall revealed that it was a ciliated epithelial cyst.

CASE REPORT

K. B., a 22-year-old white married woman, was admitted to the Tumor Service of the United States Marine Hospital on Dec. 13, 1949. She complained of difficulty in swallowing of four weeks' duration. Past history and family history were not relevant to the present illness.

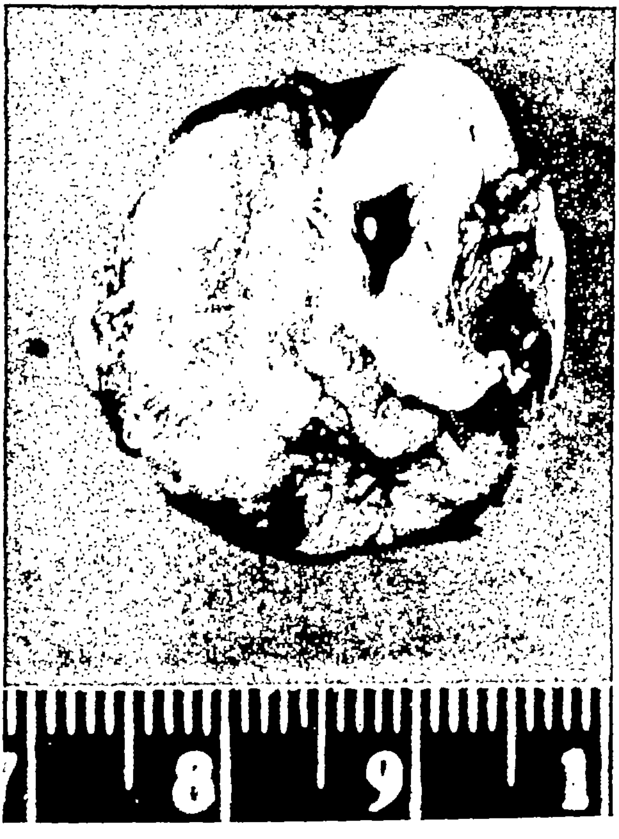

Fig. 2.—Ciliated epithelial cyst excised from the wall of the esophagus (cm. scale).

Present illness was dated from one month prior to admission when the patient first noted slight difficulty in swallowing solid foods. This dysphagia progressed and for one week before admission even liquids were swallowed with difficulty. The act of swallowing was accompanied by moderately severe substernal and epigastric pain. There had been no vomiting or regurgitation.

Physical findings were entirely within normal limits. The chest was clear to percussion and auscultation. There were no enlarged peripheral lymph nodes.

Laboratory examinations of blood and urine revealed no abnormalities.

X-ray examination of the chest was considered normal. Fluoroscopic and radiographic examinations of the esophagus with barium revealed a filling defect in the middle third of the esophagus (Fig. 1). A mass appeared to arise from the right anterior wall of the esophagus and protrude into its lumen. When large amounts of barium were swallowed the mass was displaced and permitted free passage of the meal. The radiologist believed that the mass was an intramural, extramucosal tumor of the esophagus, probably benign.

Esophagoscopy revealed the esophagus to be normal except for an area 28 cm. from the upper dental arch. Here there was bulging of the right lateral wall into the lumen but the mucosa was intact and the instrument was passed to the cardia with ease. A preoperative diagnosis of leiomyoma of the esophagus was made.

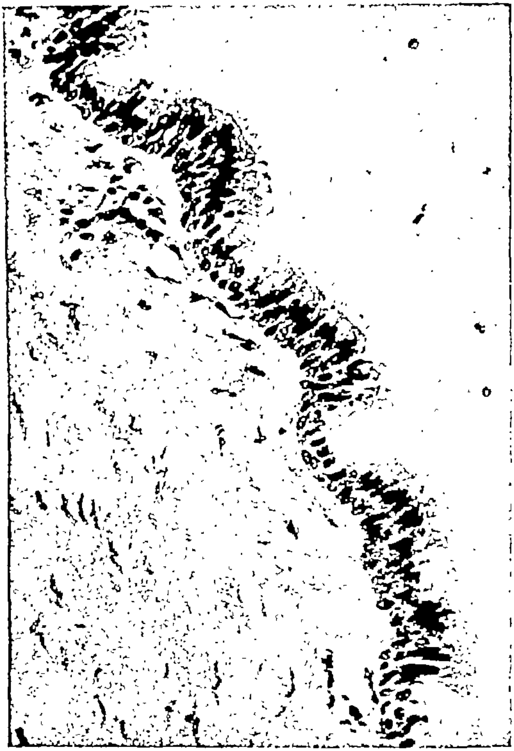

Fig. 3.—Photomicrograph, ×430, of inner fibrous portion of the cyst wall showing a lining of pseudostratified ciliated columnar epithelium.

Exploratory thoracotomy was carried out on Dec. 15, 1949. The patient was anesthetized with endotracheal nitrous oxide, oxygen, and ether, and a right posterolateral incision made. The seventh rib was resected and the right pleural space entered through its bed. The right lung was normal. In the posterior mediastinum, just below and posterior to the right main bronchus, was a cystic mass 5 cm. in diameter. The mass was intimately attached to the right anterior wall of the esophagus and the muscular coats of the esophagus expanded over the mass and lost themselves upon its surface. The mass was excised from the esophageal wall by blunt and sharp dissection. During the dissection the cyst ruptured and several drops of gray, viscid fluid oozed from the opening in its wall. The lumen of the esophagus was not entered. The muscular coats of the esophagus were approximated over the defect with interrupted sutures. The mediastinal pleura was not closed. Prior to closure of the chest a mushroom catheter was introduced through a stab wound in the fifth intercostal space.

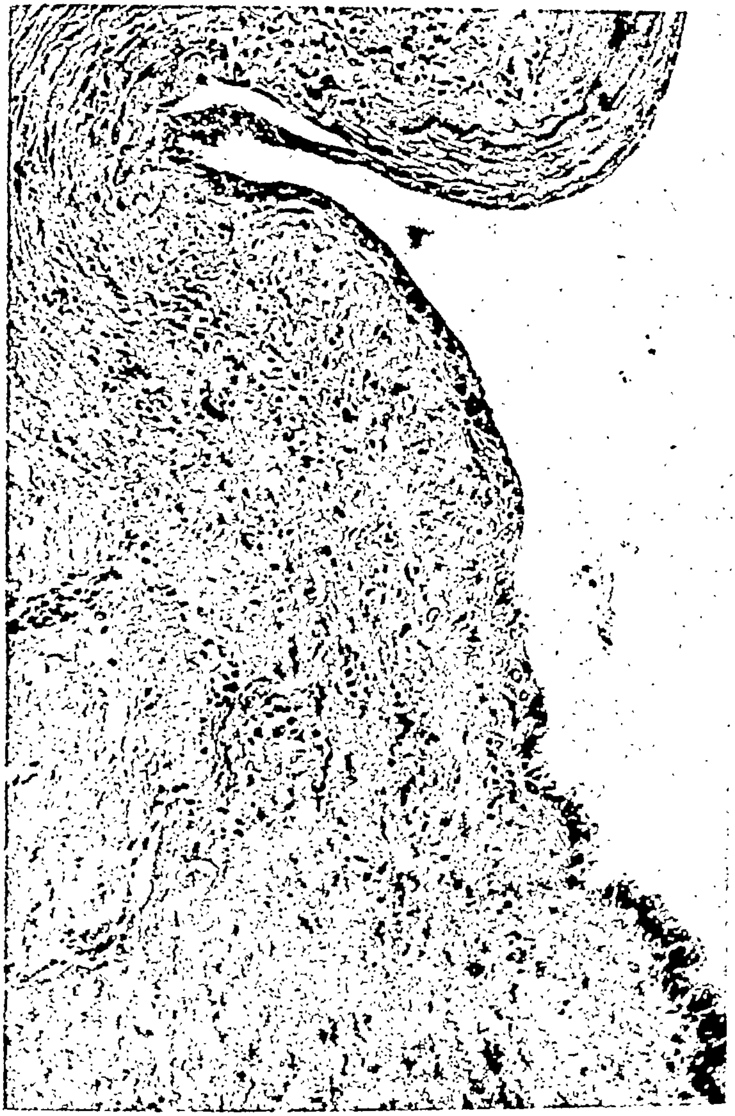

Fig. 4.—Photomicrograph, ×100, of inner portion of the cyst wall which shows a lining, on the right, of pseudostratified ciliated columnar epithelium and on the left a thin layer of stratified, relatively flat cells.

Postoperatively the catheter was connected to underwater drainage. Chest roentgenograms revealed complete expansion of the lung and the catheter was removed on the second postoperative day. The patient was given a liquid diet immediately after operation and a soft diet on the fifth day. Postoperative roentgenograms of the esophagus showed no abnormality. The patient was discharged on the thirteenth day after operation. She is well and symptom free three months after operation.

Gross Pathologic Examination.—The cysts measured 3 by 4 cm. after rupture (Fig. 2). Sectioning revealed that it contained gray gelatinous fluid. The wall was 5 mm. in thickness.

The lining of the cyst was corrugated and simulated the mucosa of small intestine. Blocks from the cyst wall were submitted for microscopic examination.

*Microscopic Examination**.—The inner portion of the cyst wall is formed of dense, sparsely cellular fibrous tissue which is hyalinized in some areas. This layer blends in an irregular fashion with the surrounding lamina of smooth muscle. In the inner fibrous portion of the wall there are scattered collections of foamy macrophages and occasional foci of lymphocytes and neutrophils. In the areas where these changes are most prominent the cyst is devoid of an epithelial lining. Elsewhere there is a lining of either pseudostratified ciliated columnar epithelium or a very thin stratified layer of relatively flat cells (Figs. 3 and 4). This latter type of epithelium is seen infrequently and in small areas. Diagnosis was ciliated epithelial cyst of the esophagus.

SUMMARY

A case of ciliated epithelial cyst of the middle one-third of the esophagus is described. The cyst caused partial obstruction of the esophagus which was relieved by transthoracic excision of the lesion.

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SURGICAL CORRECTION OF A DOUBLE AORTIC ARCH

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GREAT strides have been made recently in the diagnosis and surgical treatment of cardiovascular anomalies. For greater accuracy in diagnosis the radiograph and stethoscope have been supplemented by angiocardiography and cardiac catheterization. As a result many anomalies that formerly were case reports based upon autopsy material are now diagnosed in time for surgical correction. This report is an example of a congenital vascular ring correctly diagnosed and properly treated by ligation and division of the offending primitive arch.

In 1737, Hammel first described a case of double aortic arch and since that time over forty cases have been reported in the literature. Recently Gross and Ware, and Sweet reported four cases successfully diagnosed and operated upon with subsequent relief of the symptoms of constriction.

Embryologically a double aortic arch is the result of the persistence of both fourth branchial arches, and the fusion of the arches with the dorsal aortas to form the descending aorta. The resulting anomaly constitutes a vascular ring. The most common anatomic pattern consists of a large right aortic arch which passes to the right of the esophagus and trachea in a posterior direction, then turns to the left behind the esophagus and trachea and joins the smaller left aortic arch. On the other hand, the left aortic arch passes anterior to the esophagus and trachea and then posteriorly to join the right aortic arch. The continuation becomes the descending aorta.

In 1939, the symptomatology was nicely described by Wolman. These infants have noisy, stridorous respirations, usually noted promptly after birth, but not always. Feedings may be slow and accompanied with respiratory embarrassment in the form of dyspnea and cyanosis. In addition episodes of respiratory infection are common. Any one or all of these symptoms should suggest to the examiner the possible existence of a constricting ring.

Newhauser presented carefully studied roentgenologic findings of four cases from The Children's Hospital in Boston. He believed that there may be no abnormality on the straight posteroanterior film but in the lateral view there is narrowing and anterior displacement of the trachea at the level of the aortic arch. If the esophagus is filled with barium there appears a rounded pulsating mass posterior to the esophagus which, of course is the posterior right aortic arch displacing the esophagus forward. At the same time in the posteroanterior film the esophagus is visibly narrowed from both right and left sides due to the pressure of the vascular ring. Further if Lipiodol is instilled into the trachea it also may be narrowed in the posteroanterior diameter.

Griswold and Young have said that when a double aortic arch causes symptoms of constriction, these symptoms will develop during the first two years of

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life. Furthermore, the mere diagnosis of double aortic arch is not an indication for operative intervention. Symptoms should be present before surgery is considered.

The proper treatment is surgical division of one of the arches—thus relieving the constriction. The anterior arch is more accessible surgically and is usually smaller, but before ligation of either arch the anatomy of the vascular pattern must be carefully understood.

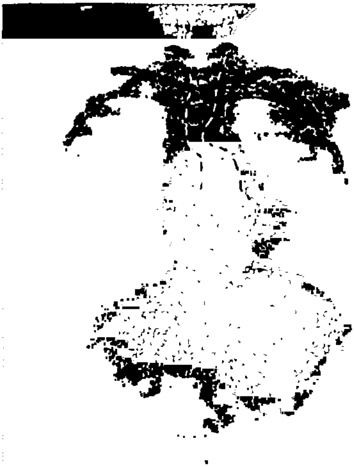

Fig. 1.—Preoperative barium swallow showing bilateral indentation of the esophagus at the level of the aortic arch. Note the dilated distal esophagus and stomach.

CASE REPORT

J. U., a 14-month-old female infant, was admitted to the Syracuse Memorial Hospital July 28, 1949, because since birth this child had had choking episodes, and difficulty in breathing associated with the feedings. Respirations were noisy and wheezy, especially when sleeping or crying. During these spells the child became blue and on occasions respirations apparently ceased. The parents kept oxygen at home for such emergencies and the assistance of the police or hospital resuscitator had been called for on several occasions. Three months before admission, while in Florida, subsequent to a severe episode, she was treated for bronchopneumonia. Three weeks before admission she was resuscitated in the emergency room of another hospital and again a diagnosis of aspiration pneumonia was made. At this admission a vascular ring was considered as a possible etiological factor by the attending pediatricians (Drs. M. P. and C. N.).

The baby had a twin and the sister was four pounds heavier and one-half inch taller. The mother stated that the other twin developed skills several weeks sooner than the patient.

Physical examination revealed a well-developed and nourished 14-month-old white female infant. She was alert and cooperative. Wheezing respirations were present and these became accentuated when the infant cried. The rest of the examination was negative.

Bronchoscopy was done on July 13, 1949, by Dr. L. S. who described a reddened trachea with definite narrowing of trachea in the anteroposterior diameter, just above the carina. Abnormal pulsations also were noted in this region.

A barium study was made of the esophagus on July 20, 1949, by Dr. C. H. Radiographic and fluoroscopic examination of the chest and esophagus showed that there was definite narrowing of the esophagus at the level of the aortic arch. The narrowing was bilateral, and the defect was typical of a congenital aortic ring. The nature of the deformity of the esophagus suggested that the vascular anomaly was a double aortic arch. The distal esophagus was dilated as was the stomach (Fig. 1).

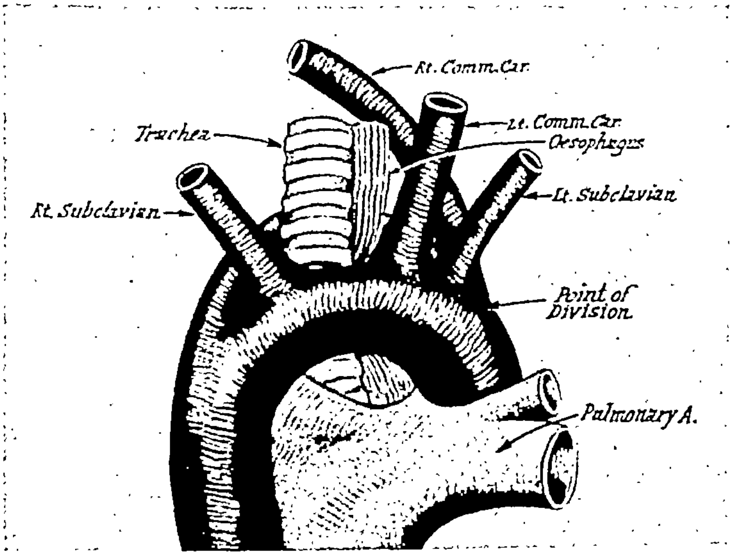

Fig. 2.—Sketch of the anatomy as found at operation.

Conclusion was that the examination of the esophagus showed definite deformity due to a vascular ring. The vascular anomaly was probably a double aortic arch. The cardiac shadow was normal. There was no evidence of disease in the lungs.

Exploratory thoracotomy was performed on Aug. 1, 1949.

Patient was given rectal anesthesia and intratracheal general anesthesia. Blood was started immediately in the right ankle. Patient was placed on her right side, and the left chest was prepared and draped in the usual manner for a thoracic operation. Usual posterolateral incision was made in the left fifth intercostal interspace. The fourth and fifth ribs were fractured at their posterior attachment. A rib-spreader was introduced. The pleura on the left lateral surface of the superior mediastinum was opened, and dissection was begun above the aortic arch. The left common carotid and left subclavian arteries were isolated, and tapes were placed around them for traction. The arch of the aorta was completely exposed and an anomalous blood vessel was found to arise from the ascending aorta. This vessel was isolated by further dissection and was found to have one branch which went cephalad and was thought to be the right subclavian artery. Another branch went around the esophagus and trachea and reunited with the arch of the aorta to the left of the esophagus. This vessel formed a complete vascular ring about the esophagus and trachea.

Caudad to this vascular ring, the esophagus was bulbous and dilated. Posterior to the esophagus and the trachea, this anomalous vessel was closely adherent to these structures. A large artery arose from the posterior arch to the left of the esophagus and passed obliquely to the right. It was considered to be the right common carotid artery. Finally, it was decided that it would be easier to transect the vascular ring anteriorly for technical reasons, since the exposure posteriorly would be difficult to obtain (Fig. 2).

The anterior arch of the aorta was temporarily clamped at a point just proximal to the common aorta. The circulation to all carotid and subclavian vessels remained good. Therefore it was decided to transect the arch of the aorta anteriorly. The anterior arch, just in front of the esophagus, was then doubly ligated with No. 3 silk, and divided. Subsequent to the division the ends spread laterally for a distance of 4 cm., and both the trachea and esophagus moved forward. Therefore, it was felt that the vascular ring, which had constricted the esophagus, was definitely released.

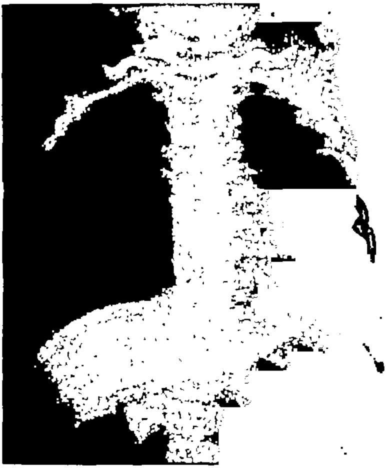

Fig. 3.—Postoperative barium swallow.

The pleural cavity was then irrigated and hemostasis checked. The superior mediastinum was not repleuralized. The thorax was then closed in anatomic layers. A rubber tube was placed low in the pleural cavity, (connected to a "water seal" for drainage) to maintain re-expansion of the lung. The patient tolerated the procedure very well. She received 350 c.c. of blood on the table and was returned to her room in good condition. The postoperative course was uneventful. Some stridor was present for several days, which was considered to be laryngeal edema due to the endotracheal tube. The child was discharged on the eighth postoperative day in good condition. Since discharge from the hospital she has gained weight and is now the same size as the twin sister. The mother states that she can no longer tell which twin is crying. Feedings are normal and uneventful.

On Jan. 11, 1950, a repeat barium swallow was reported. Complete radiographic and fluoroscopic examination of the chest revealed the heart to be of normal size, shape, and position. The lung fields were clear. There was no evidence of active pulmonary disease.

The fifth and sixth ribs on the left posteriorly showed moderate callous formation following fracture due to a thoracotomy. The barium passed freely through the esophagus into the stomach. There was no evidence of constriction or deviation. There was the normal concave marking that we see at the level of the aorta. The lumen was of normal caliber throughout. There was no posterior defect on the esophagus as one sees when there is a double aortic arch or a right aortic arch. The stomach was filled with air, but was of normal size for a patient of this age (Fig. 3).

Conclusion was that the heart and lung fields were normal. The esophagus was of normal caliber throughout, and there was no evidence of stricture or defect around the region of the previous surgery.

SUMMARY

A case of double aortic arch is presented which was correctly diagnosed and successfully treated by operation. The diagnosis is suggested from the history and physical findings, and is easily confirmed by bronchoscopic and roentgenologic studies. The only treatment is surgical correction by division of one arch.

I should like to express my appreciation to Dr. J. W. Chamberlain and Dr. William Michaels for valuable help given.

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THE BLOOD FLOW THROUGH AN ATELECTATIC LUNG

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AS SOON as an atelectasis has developed, the blood flow through this area is considerably decreased. During the first days and weeks this decrease in blood flow through an atelectatic part has been estimated to be about 50 per cent of the normal (Moore, 1931, and Berggren, 1942). With the aging of the atelectasis there will be a continued decrease in flow until practically no blood at all is passing the atelectatic parts.

In an acute atelectasis all venous blood from the nonventilated parts of the lung is mixed with fully oxygenated blood, thus reducing the oxygen content of the arterial blood. The arterial oxygen deficit, which is most pronounced in the acute atelectasis, will diminish at the same rate as the blood flow through the atelectatic part decreases.

The decreased blood flow in the atelectatic part of the lung might be produced by contraction of the large branches of the pulmonary artery or by collapsed capillaries around the empty alveoli. Some clinical findings speak in favor of the latter possibility. In three cases with a total tuberculous stenosis of one main bronchus, a thoracoplasty had been performed one, two, and four years previously. No arterial oxygen deficit was found with the lung breathing air or 100 per cent oxygen. When the pneumonectomy was performed the pulmonary artery to the atelectatic lung was found to be larger than expected and nearly of normal size. Furthermore, it is well known that the capillaries close down in a resting part of an organ.

EXPERIMENTAL FINDINGS

Some experiments were performed to produce atelectasis in the dog. The blood flow through the atelectatic part of the lungs was demonstrated by angiocardiography and the arterial oxygen deficit was determined.

Acute Atelectasis

During intravenous narcotal anesthesia acute atelectasis of the right lung of a dog weighing 13 kilograms was produced with the aid of a Carlens double-lumen catheter for bronchospirometry. Each lung was then breathing separately. While the left lung was breathing ordinary air, the right was first breathing 100 per cent oxygen and was then connected to a valve only permitting the outflow of gas, but no inflow.

The development of the atelectasis was followed by x-ray investigation at fifteen-minute intervals. After two hours the x-ray picture showed a pronounced atelectasis of the right lung with mediastinal shift and the right border of the heart only 1 cm. from the right chest wall. Still the right lower lobe was

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air-containing. With this partial atelectasis of approximately one-half of the right lung the arterial oxygen content was investigated (according to Van Slyke and Neil): there was partial atelectasis of the right lung; the left lung breathing air equaled 89.5 per cent arterial oxygen saturation; the left lung breathing 100 per cent oxygen equaled 95.9 per cent arterial oxygen saturation.

Then a complete atelectasis of the right lung was obtained by applying continuous strong suction (with a vacuum cleaner) to the right tube of the double-lumen catheter. The roentgenogram showed a total atelectasis of the right lung with the right border of the heart out at the right chest wall (see Fig. 1).

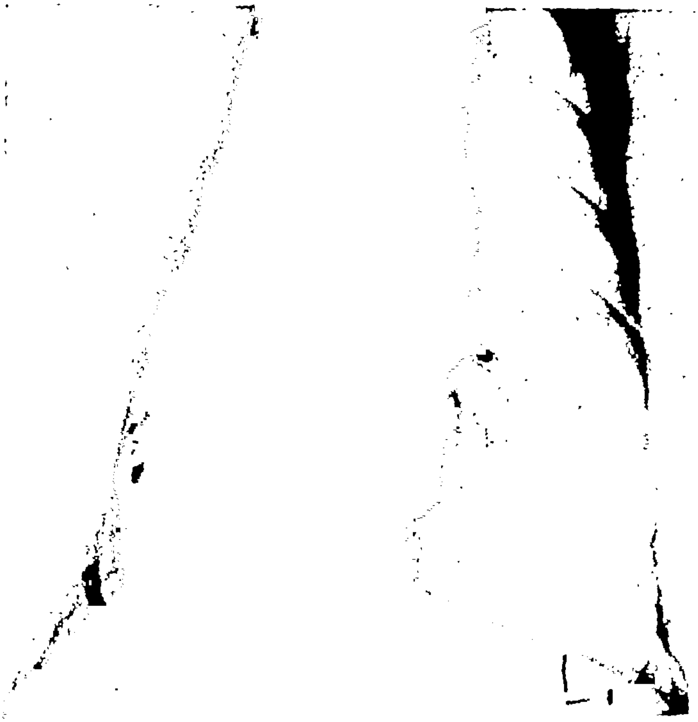


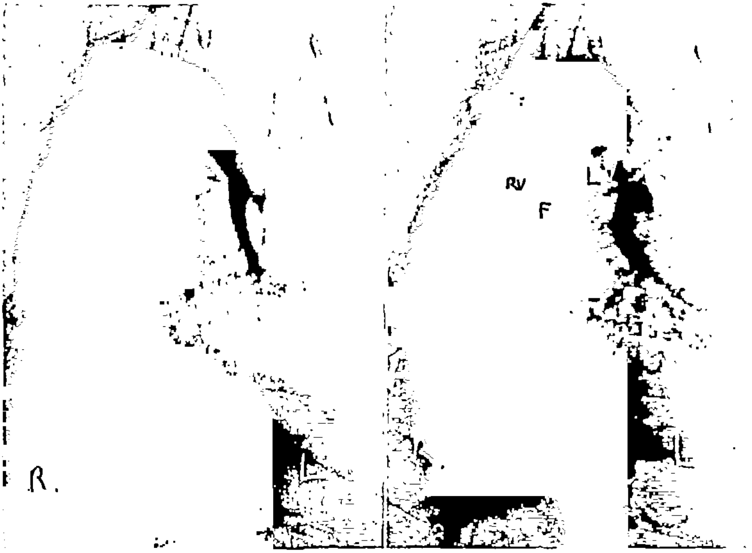
Fig. 1.—Total acute atelectasis of the right lung.

A heart catheter was now introduced through the right external jugular vein, through the right side of the heart out into the pulmonary artery. Angiocardiography was then performed by injection of 40 ml. 70 per cent *Diodrast* with an over-pressure syringe (according to Jönsson). Six x-ray films were automatically exposed at intervals of one second. Simultaneous exposures in right angle planes were not taken in order to avoid the disturbance of secondary radiation.

The angiocardiography showed approximately the same size of the peripheral branches of the pulmonary arteries on both sides (see Fig. 2, *A*). Some seconds later one of the left pulmonary veins (*LV*) was clearly visible at the same time as one right upper pulmonary vein (*RV*) emptied into the left auricle (*F*) (see Fig. 2, *B*). The amount of contrast in the periphery of the right atelectatic lung seemed to be greater than in the left lung.

Conclusion.—In an acute atelectasis the pulmonary arteries do not get smaller and the capillary bed remains open as indicated by the contrast filling of pulmonary arteries and veins simultaneously on both sides. The contrast filling of the periphery of the atelectatic lung is at least as pronounced as on the other side.

The arterial oxygen content during total acute atelectasis of the right lung was investigated: there was total atelectasis of the right lung; the left lung breathing 100 per cent oxygen equaled 88.0 per cent arterial oxygen saturation, 36.2 volumes per cent carbon dioxide.



A. *B.*

Fig. 2.—*A*, Angiocardiography shows the same size of the peripheral pulmonary artery branches during acute atelectasis of the right lung as compared with the ones of the distended left lung.

B, Both left (*LV*) and parts of the right pulmonary veins (*RV*) are filled with contrast medium, emptying into the left auricle (*F*). The contrast filling of the periphery of the atelectatic right lung seems somewhat more pronounced than on the left side.

To see the influence of the atelectasis on the flow of blood through nonventilated parts of the lungs, the following experiment was performed:

The right lung was again freely ventilated when the atelectasis completely disappeared. The roentgenogram showed the heart in the normal position, the trachea in the middle, and an air-containing right lung. Then the right lung was made to breathe 100 per cent nitrogen for fifteen minutes when the arterial oxygen content was investigated: the right lung breathing 100 per cent nitrogen; the left lung breathing 100 per cent oxygen equaled 85.9 per cent arterial oxygen saturation, 36.3 volumes per cent carbon dioxide.

Conclusion.—The loss of oxygen from the blood in the lung breathing 100 per cent nitrogen can be considered compensated by the other lung. An approximately equal arterial oxygen deficit is found with complete atelectasis of one lung as compared with the same lung breathing 100 per cent nitrogen. This indicates that the decrease of blood flow due to an acute atelectasis is of the same order as that due to the increased resistance in the capillary bed of a lung breathing 100 per cent nitrogen. Still a considerable amount of blood is passing through the nonventilated area in the acute stage of an atelectasis.

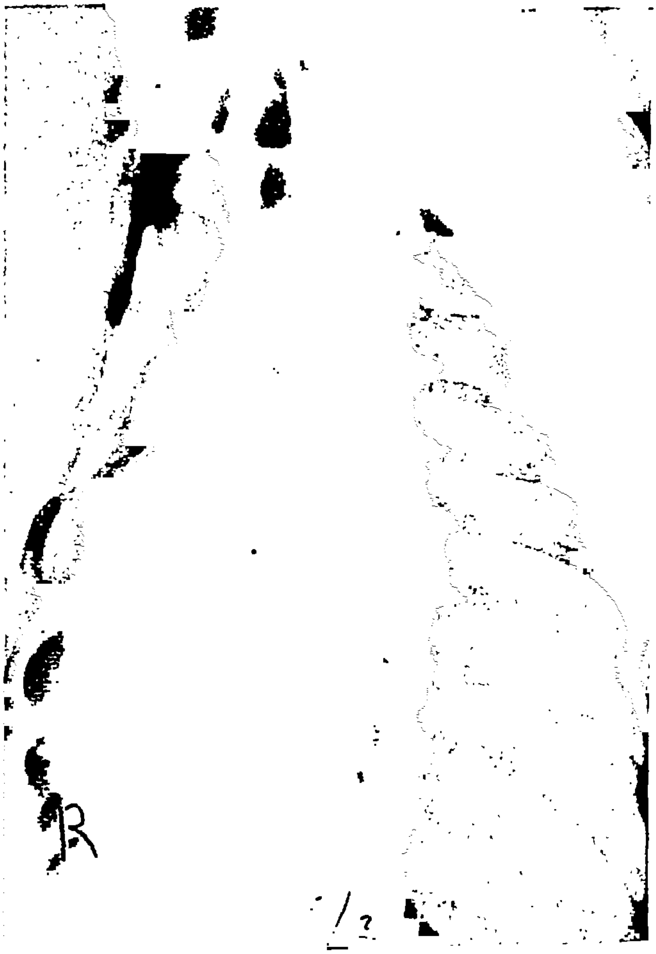


Fig. 3.—Total atelectasis of the right lung with mediastinal shift and a remaining pneumothorax.

Chronic Atelectasis

Chronic atelectasis was produced by ligation of all bronchi to the right lung. After a premedication of 1 cg. of morphine with scopolamine the anesthesia was induced with narcotal intravenously on a dog weighing 22 kilograms. An intratracheal tube was then introduced and positive pressure anesthesia continued with ether and oxygen using the spiro-pulsator. The right chest was opened after resection of most of the fourth and the posterior part of the fifth ribs. The azygos vein was divided between ligatures and trachea with the right main bronchi was dissected free. The right upper lobe bronchus was found to leave the right main bronchus at the same level as the carina and had to be ligated separately. Then the main bronchus to the rest of the right lung could be isolated and tied with a thick ligature (boot-laces were used to prevent cutting through). The wound was closed and air aspirated from the right chest.

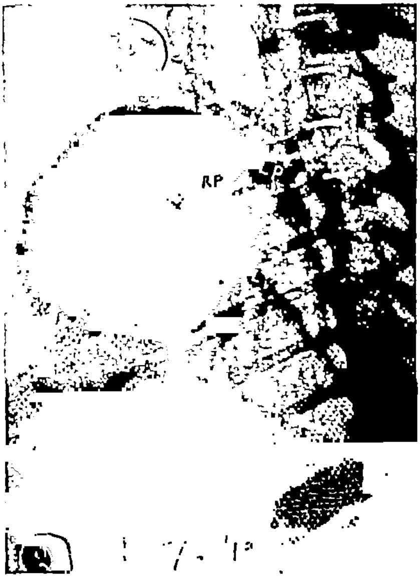


Fig. 4.—Lateral angiocardiography shows right (*RP*) and left pulmonary artery (*LP*) to be of the same size after total atelectasis of the right lung for twenty-four hours. *LV* is the left pulmonary vein.

Twenty-four-hour Atelectasis.—The day after the operation the dog was in good condition and running around. Roentgenogram showed a total atelectasis of the right lung with mediastinal shift to the right. There was a remaining pneumothorax on the operated side but no compression from exudate (see Fig. 3). All arterial samples for analyses were taken under intravenous narcotal anesthesia and after insertion of an intratracheal tube. The first sample was taken when the dog was breathing air. The second sample was taken when the dog had been breathing 100 per cent oxygen for fifteen minutes. The connection to the intratracheal tube was fitted with an expiratory valve permitting the expiratory air to escape. Blood gas analyses were performed according to the Van Slyke and Neill manometric method with double determinations of the oxygen content as well as of the oxygen capacity of each sample. Blood analysis

after twenty-four-hour atelectasis showed: lung breathing air equaled 81.0 per cent arterial oxygen saturation, 36.7 volumes per cent carbon dioxide; lung breathing 100 per cent oxygen equaled 93.6 per cent arterial oxygen saturation, 37.2 volumes per cent carbon dioxide.

Angiocardiography with a ventrodorsal x-ray direction was performed according to Robb-Steinberg, with injection of 40 ml. 80 per cent Umbradil in a hind-leg vein. The vessels in the atelectatic right lung could not be seen due to the contrast medium filling of the heart.

Another angiocardiography was now performed using the same Robb-Steinberg technique injecting 40 ml. 80 per cent Umbradil, but with the dog in a slightly rotated lateral position. The main right pulmonary artery (*RP*) to the atelectatic lung was found to be of the same size as the left pulmonary artery (*LP*). The lower left pulmonary vein (*LV*) was also visible (see Fig. 4).

Three-day Atelectasis.—After three-day total atelectasis of the right lung, x-ray investigation showed an increased distention of the left lung (see Fig. 5). Blood analysis showed: lung breathing air equaled 76.5 per cent arterial oxygen saturation, 41.4 volumes per cent carbon dioxide; lung breathing 100 per cent oxygen equaled 97.1 per cent arterial oxygen saturation, 43.1 volumes per cent carbon dioxide.

Angiocardiography showed the same picture as Fig. 4, with the same size of the right and left pulmonary artery.

Six-day Atelectasis.—After six-day total atelectasis of the right lung, blood analysis showed: lung breathing air equaled 83.0 per cent arterial oxygen saturation, 45.7 volumes per cent carbon dioxide; lung breathing 100 per cent oxygen equaled 94.8 per cent arterial oxygen saturation, 38.0 volumes per cent carbon dioxide.

Twelve-day Atelectasis.—Blood analysis showed: lung breathing 100 per cent oxygen equaled 92.4 per cent arterial oxygen saturation, 44.6 volumes per cent carbon dioxide.

Twenty-four-day Atelectasis.—Blood analysis showed: lung breathing 100 per cent oxygen equaled 100.5 per cent arterial oxygen saturation. No arterial oxygen deficit remained, lung breathing *100 per cent oxygen.*

One-month Atelectasis.—Angiocardiography showed the same picture as in Fig. 4, with the same size of the right and left pulmonary artery.

Eight-month Atelectasis.—Blood analysis showed: lung breathing air equaled 66.8 per cent arterial oxygen saturation; lung breathing 100 per cent oxygen equaled 97.3 per cent arterial oxygen saturation.

Angiocardiography was performed through a heart catheter inserted through the left external jugular vein into the pulmonary artery; 50 ml. 70 per cent Umbradil were injected with an over-pressure syringe. With the dog in a slightly rotated lateral position, a considerable decrease in the size of the right main pulmonary artery was demonstrated (see Fig. 6, *A*). On the x-ray picture the diameter of the main right pulmonary artery measured 9 mm., as compared with a diameter of 15 mm. of the left pulmonary artery. The corresponding diameters were equal or 15 mm. on both sides after one-month atelectasis.

Another angiocardiography was then performed with a dorsoventral direction of the roentgenograms, but otherwise with the same technique. The right pulmonary artery was found to have decreased in size when compared with the left pulmonary artery (see Fig. 6, *B*).

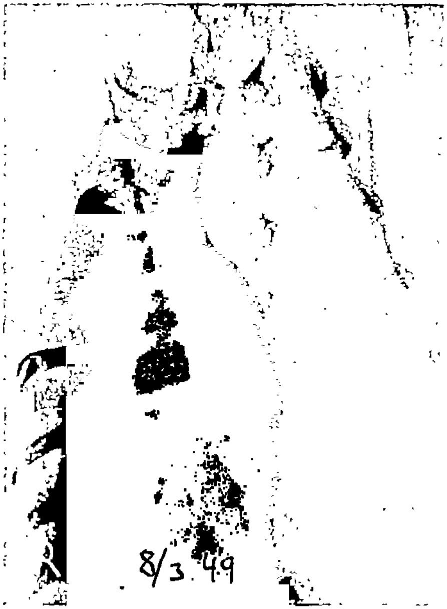


Fig. 5.—Roentgenogram after total atelectasis of the right lung for three days.

One second later the contrast medium has passed through the left pulmonary artery and is filling the left pulmonary veins. At the same time on the right side the right pulmonary artery is still filled with contrast, but no contrast medium is visible in the right pulmonary veins (see Fig. 6, *C*).

Autopsy was then performed showing a complete obstruction of all bronchi to the total atelectatic right lung. All pulmonary arteries and veins had a macroscopically normal appearance. Microscopic investigation showed atelectasis of the right lung with no signs of fibrosis.

In two cases of bronchial occlusion with atelectasis of the right upper lobe due to bronchiogenic carcinoma the following values were found. Atelectasis

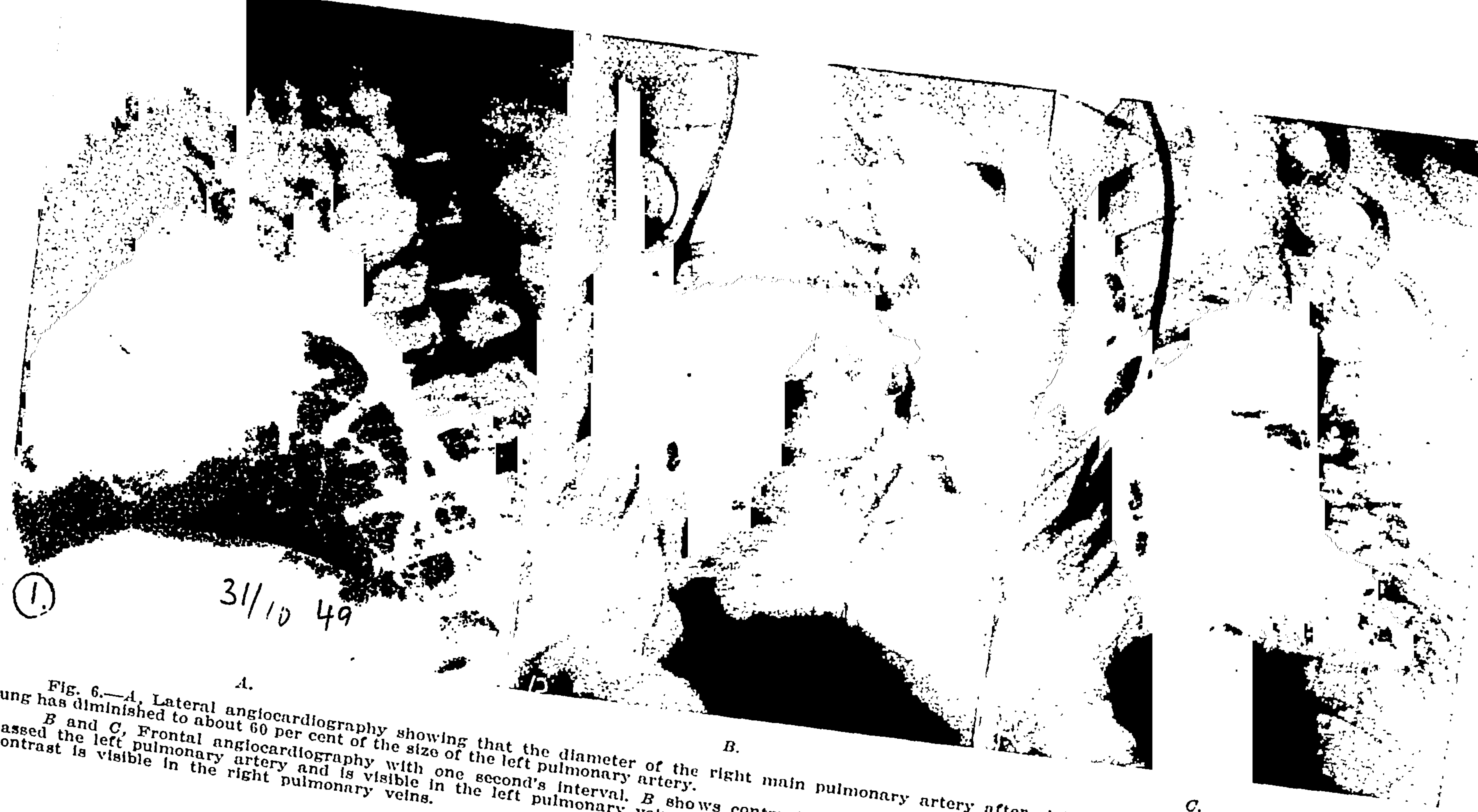


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Fig. 6.—*A*, Lateral angiocardiography showing that the diameter of the right main pulmonary artery after eight-month total atelectasis of the right lung has diminished to about 60 per cent of the size of the left pulmonary artery.

B and *C*, Frontal angiocardiography with one second's interval. *B* shows contrast in the pulmonary arteries on both sides. In *C* the contrast has passed the left pulmonary artery and is visible in the left pulmonary veins. At the same time the right pulmonary artery is still filled with contrast. No contrast is visible in the right pulmonary veins.

of right upper lobe for more than six weeks: breathing air equaled 88.5 per cent arterial oxygen saturation; breathing 100 per cent oxygen equaled 98.8 per cent arterial oxygen saturation. Atelectasis of right upper lobe for about two weeks: breathing air equaled 91.4 per cent arterial oxygen saturation; breathing 100 per cent oxygen equaled 95.2 per cent arterial oxygen saturation.

Conclusion.—In chronic atelectasis the blood flow through the nonventilated areas of the lungs diminishes with the age of the atelectasis. At the same time the arterial oxygen deficit diminishes with the lung breathing 100 per cent oxygen. No arterial oxygen deficit remained after total atelectasis of the right lung of a dog for twenty-four days. In one case of bronchiogenic carcinoma with right upper lobe atelectasis for two weeks an arterial oxygen deficit remained. In a similar case of more than six weeks' duration, there was practically no arterial oxygen deficit with the lung breathing 100 per cent oxygen.

During the first month of an atelectasis the arterial oxygen deficit is greatly diminished or disappearing. The blood flow through the nonventilated parts is diminishing at the same rate. When the greatest change in the blood flow through the atelectasis is to be found, the corresponding artery has not at all diminished in size.

After eight-month atelectasis the corresponding pulmonary artery had diminished in size, but still its diameter was 60 per cent of the contralateral pulmonary artery. The contrast medium in the artery of the atelectatic lung did not empty at the same time as on the other side, and no pulmonary veins were filled.

The blood flow through atelectatic parts of the lungs is therefore thought to be shut off in the capillaries. The large branches of the pulmonary artery are filled with slowly circulating blood, which passes either not at all or extremely slowly through the capillary bed of the atelectatic area.

SUMMARY

In an acute atelectasis the pulmonary arteries do not become smaller, and the capillary bed remains open as indicated by contrast medium simultaneously filling pulmonary arteries and veins on both sides. The contrast filling of the periphery of the atelectatic lung is at least as pronounced as on the other side. An approximately equal arterial oxygenation deficit with complete atelectasis of one lung as compared with the same lung breathing 100 per cent nitrogen is found. This indicates that the decrease of blood flow due to an acute atelectasis is of the same order as that due to the increased resistance in the capillary bed of a lung breathing 100 per cent nitrogen. Still a considerable amount of blood is passing through the nonventilated area in the acute stage of an atelectasis.

The blood flow through an atelectatic area is continuously decreasing during the first month, until practically no blood is passing through the nonventilated part of the lungs. At the same time there is no decrease in size of the main branches of the corresponding pulmonary artery. Therefore, the blood flow is thought to be shut off in the capillary bed, which is gradually closing down.

In a long-standing atelectasis the pulmonary artery will decrease somewhat in size. The contrast medium does not disappear from the artery in the atelectatic part in the same time as on the healthy side, nor are the pulmonary veins filled with contrast medium in the atelectatic part at the same time as on the healthy side. The blood, therefore, is considered to fill out the arteries of the atelectatic lung but to pass either not at all or extremely slowly through the capillary bed. The capillaries are considered to be closed down in the same way as in a resting part of an organ.

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WOUND HEALING FOLLOWING LIMITED RESECTION OF THE PARIETAL PLEURA

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THE surgical removal of pleural membranes that limit pulmonary expansion was popularized during World War II as appropriate treatment for sterile and contaminated fibrothoraces following pleural injury.[3, 7] The procedure was applied subsequently to visceral pleura thickened by tuberculosis.[1, 2] Sarot has reported extrapleural total or partial resections of the lung with simultaneous removal of affected visceral and parietal pleura for pulmonary and pleural tuberculosis.[4, 5] Tchertkoff and Selikoff noted fewer complications after extrapleural pneumonectomy than after transpleural removal of the lung.[6]

With increasing interest in the role of the pleura in intrathoracic surgery as well as the healing processes of the endothorax following pleural denudation, the following study was performed to determine tissue repair after limited pleural resections.

METHOD

Under intratracheal ether anesthesia, thoracotomies were performed on adult cats through the sixth intercostal space. Since it is difficult to remove a desired portion of normal pleura from the cat without shredding, a segment of pleura was excised from the anterior thoracic wall with the adjacent transverse thoracic muscle. A uniform lesion, measuring 2 by 1 cm. was made and the parietal defect was outlined by silk stitches for later identification. The chest wound was closed in layers about a catheter using silk technique. The lung was re-expanded on the operating table with the aid of positive intratracheal pressure, the catheter and water-seal drainage. After maximal expansion, the catheter was removed and closure of the wound was completed.

Animals were killed at intervals from the second to the twenty-eighth postoperative days. There was no incidence of empyema and all cats did well following operation. At autopsy, the pleural wounds were removed and sections were prepared with hematoxylin and eosin and Masson's trichrom stains.

RESULTS

Gross.—During the first postoperative week, the surface of the wound was smooth and dull. There was edema of the surrounding pleura up to the fifth day. The wound was depressed, probably because muscle was removed with the pleura at the time of resection. After the first week, the lesion became progressively more glistening and at the end of two weeks, interlacing fibrous strands crossed the defect. No contraction of the wound was observed.

Adhesions were absent on gross examination. This was due perhaps to partial pneumothorax during the early postoperative period. There was also

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moderate gliding motion of the lung over the anterior chest which would prevent adhesions at the site of such a minor injury.

Microscopic.—Two days after operation the parietal wound was covered with a thin layer of fibrin that extended over the adjacent normal pleura. Beneath this was a vacuolated layer of fibrin containing a small number of leucocytes (Fig. 1). Most of these were mononuclear although a significant number of polymorphonuclear cells were present. These cells infiltrated the subjacent fat, facial and muscle planes which were edematous. The edge of the wound was well delineated by the discontinuity of the subpleural collagen layer.

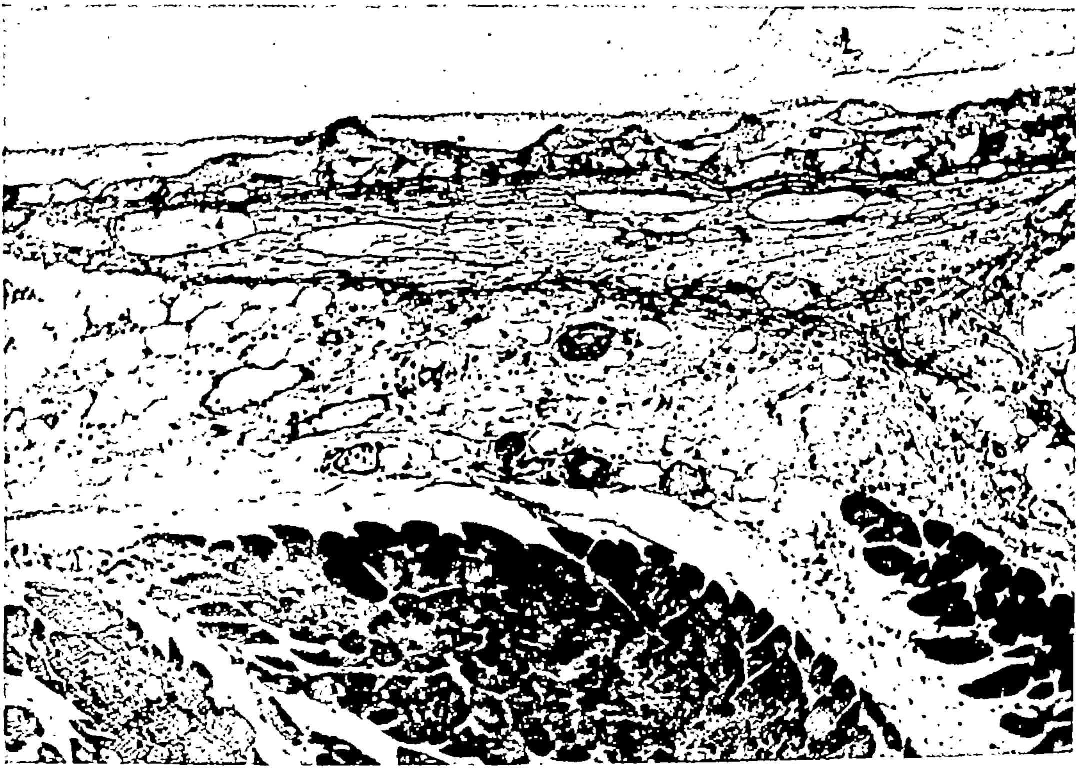

Fig. 1.—Pleural wound two days after operation. Note irregular fibrin layer containing few inflammatory cells. ×124.

Leucocytic infiltration of the wound and adjacent tissues gradually increased up to the fifth day. Mononuclear cells predominated. There was progressive thickening of the overlying fibrin layer during this period. On the fifth day the fibrin over the wound was laminated. Inflammatory cells were still present in the deeper structures, but the amount of tissue edema was diminished. There were many fibroblasts in the deeper layers of the surface exudate. They bordered the interstices of the laminated fibrin and were occasionally on the wound surface. They were particularly numerous near the edges of cut muscle. Many fibroblasts were undergoing mitosis (Fig. 2).

Fibroplasia subsequently was progressive so that by the ninth day, the wound was covered by smooth, cellular, fibrous tissue (Fig. 3). Fibrin was absent, but there were tiny capillaries in the deeper layers. A single layer of

ALVEOLAR-CELL TUMORS OF THE LUNG[*]

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ALVEOLAR-CELL tumors of the lung are recognized as one of the rare pulmonary neoplasms. In recent years scattered cases have been reported under two common headings: "alveolar-cell carcinoma" and "pulmonary adenomatosis." Malassez[1] reported the first case of nodular alveolar-cell carcinoma in 1876, and in 1903, Musser[2] described the first case of diffuse alveolar-cell carcinoma. In 1907, Helly[3] reported the first case of pulmonary adenomatosis. The lessions in all these cases were morphologically the same. From this time to April, 1949, 51 acceptable cases of pulmonary alveolar-cell tumors were reported under the two headings given above. However, the etiology of these neoplasms still remains a topic for heated debate among the histopathologists. Until definite proof can be established that these pulmonary tumors are derived from either ectodermal or mesenchymal tissue, the term "alveolar-cell tumor," first introduced by Neubuerger,[4] is still the most acceptable name.

Pulmonary alveolar-cell tumor in man is only one of many pathologic conditions in which cells line the alveolar spaces. In 1943, Geever, Neubuerger, and Davis[5] outlined fifteen general conditions in man and animals in which the alveoli were lined with epithelial-like cells. The disease, jagziekte, of sheep is mentioned by many authors as being similar to alveolar-cell tumors in man. However, jagziekte is seen mainly in Africa, Europe, Montana, and Iceland. From Dungal's[6] report, in 1946, it appears almost certain that this is an infectious disease which is not transferable to man. It is true that the microscopic picture of jagziekte is similar to that of alveolar-cell tumor in man, but this is also true of many types of pneumonia.

MATERIAL AND METHODS

The first case of surgically excised alveolar-cell tumor of the lung (Case 1) was encountered at the Mayo Clinic in 1943. Since then there have been 6 other cases in which operation was performed. The clinical history, laboratory reports, and pathologic aspects were studied in these 7 cases. Special stains were used on the resected pulmonary tissue, including hematoxylin and eosin, Gömöri reticulum, mucicarmine, Sudan IV, and van Gieson stains. The cells of each tumor were graded on a basis of 1 to 4 to designate their relative state of anaplasticity, grade 1 representing the least change and grade 4 the greatest change.

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REPORT OF CASES

CASE 1.—A 54-year-old woman first registered at the Mayo Clinic on Feb. 3, 1943, because of a severe nonproductive cough which had been present for one year. During this period she lost twelve pounds (5.4 kilograms). She gave a history of tuberculosis in the family. The erythrocytes numbered 4,730,000 and the leucocytes 6,200, the hemoglobin measured 13.1 Gm., the sedimentation rate was 32, roentgenograms of the thorax revealed a pathologic process at the base of the left lower lobe, and multiple tests for tuberculosis gave negative results. Bronchoscopy also gave negative results. No cytologic examination was made.

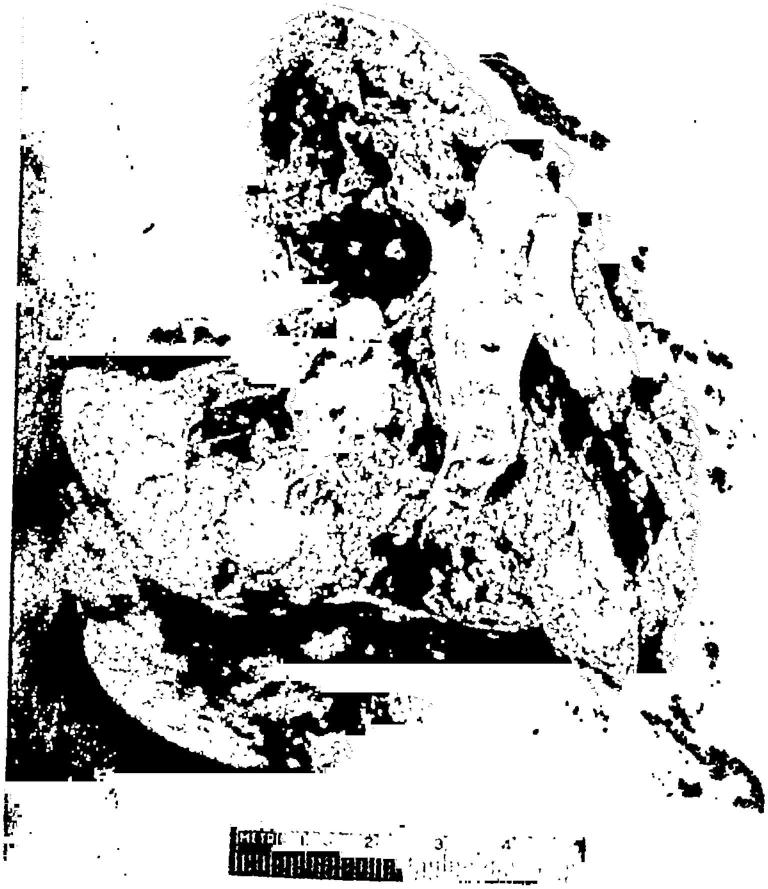

Fig. 1 (Case 1).—Alveolar-cell tumor of the nodular type involving the lower left lobe. Multiple mucoid-appearing nodules are present.

Left lower lobectomy was done on Feb. 15, 1943, by one of us (Clagett). No evidence of metastasis was found in the left side of the thorax at operation. The entire lobe was replaced by a pinkish mass, which on cut surface was composed of nodules that tended to become confluent (Fig. 1). The pleura was not involved. The cut surface of the tumor was glistening. Histologically the picture was that of a typical alveolar-cell tumor with the cells showing only a moderate degree of irregularity (grade 2). Numerous cells contained mucus (Fig. 2). The stain for fat showed fat in the interalveolar septa but none in the tumor cells. There were numerous lipophages in the neoplastic as well as in the nonneoplastic alveoli. The reticulum stain revealed that the alveolar septa were intact in the region of the tumor. The patient died on the fifth postoperative day of myocardial infarction. Necropsy disclosed no tumor in the lobes of the right or left lung. There was no metastasis elsewhere.

CASE 2.—A 55-year-old white woman gave a history of nonproductive cough and dyspnea of two years' duration. Nine months prior to admission, after an attack of influenza, she noticed that she was having a great amount of fatigue. One month before admission she began to notice progressive anorexia and nocturnal dyspnea. Shortly thereafter, she began having nausea, vomiting, chills, and fever. Two days prior to admission her cough became productive of blood and pus. This was followed by pain in the left upper part of the thorax. She gave no history of loss of weight. Her past history was noncontributory except for pneumonia several years prior to admission. On physical examination the border of the liver was palpable and the blood pressure was 178 systolic and 94 diastolic expressed in millimeters of mercury. Otherwise the examination gave negative results. The erythrocytes numbered 4,830,000, the leucocyte count was 4,800, a serologic reaction for syphilis was negative, the hemoglobin content was 14.2 Gm. per 100 c.c. of blood, the sedimentation rate was 46 mm. in one hour (Westergren), urinalysis gave negative results, and the acid-fast stain did not disclose any tubercle bacilli but cytologic examination of the sputum revealed carcinoma cells that appeared to be of the alveolar-cell type. Roentgenograms gave evidence of pneumonitis of the lingular portion of the left upper lobe. Bronchoscopy gave negative results.

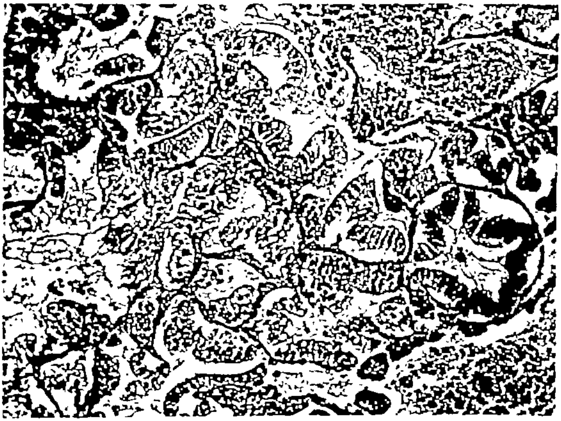

Fig. 2.—Same case as in Fig. 1. Numerous cells contain mucus. Multiple lipophages in the alveoli (hematoxylin and eosin, ×125).

Left upper lobectomy was performed. At operation no evidence of metastasis was found. Grossly the lingular portion of the upper lobe was involved with pinkish-white tumor which appeared nodular on cut surface. There was no pleural involvement. Microscopic examination revealed typical alveolar-cell tumor with moderate irregularity of the nucleoli (grade 2). The mucicarmine stain gave mildly positive results. The reticulum stain showed intact alveolar septa. The stain for fat disclosed a large amount of fat in the alveolar septa but none in the cells.

The patient was living and well six months after operation, with complete relief of cough and dyspnea.

CASE 3.—A 47-year-old white woman was admitted with the history that a severe attack of bronchitis had occurred four years previously. Two years before admission, a severe productive cough developed; this was accompanied by one episode of hemoptysis. Penicillin therapy was instituted with relief of symptoms. Seven months before admission she again had a cough that was productive of watery sputum and was accompanied by substernal discomfort after coughing. All studies for tuberculosis gave negative results. On physical examination the left lower part of the thorax was dull to percussion, and a few râles were present. She gave a history of having had pneumonia three times and pleurisy three times. The erythrocytes numbered 4,610,000, the leucocyte count was 5,700, a serologic reaction for syphilis was negative, urinalysis gave negative results, the sedimentation rate was 18, the hemoglobin content was 10.8 Gm., and the roentgenogram showed an area of pneumonitis in the left lower pulmonary field. Bronchoscopic examination gave negative results. Cytologic examination was reported as giving negative results at that time, but later the cells seen in the sputum were classified as carcinoma cells. Left lower lobectomy was performed. At the time of operation no evidence of metastasis was found. On gross examination the lower four-fifths of the lobe was solidified and airless and was replaced by a pinkish-white tumor.

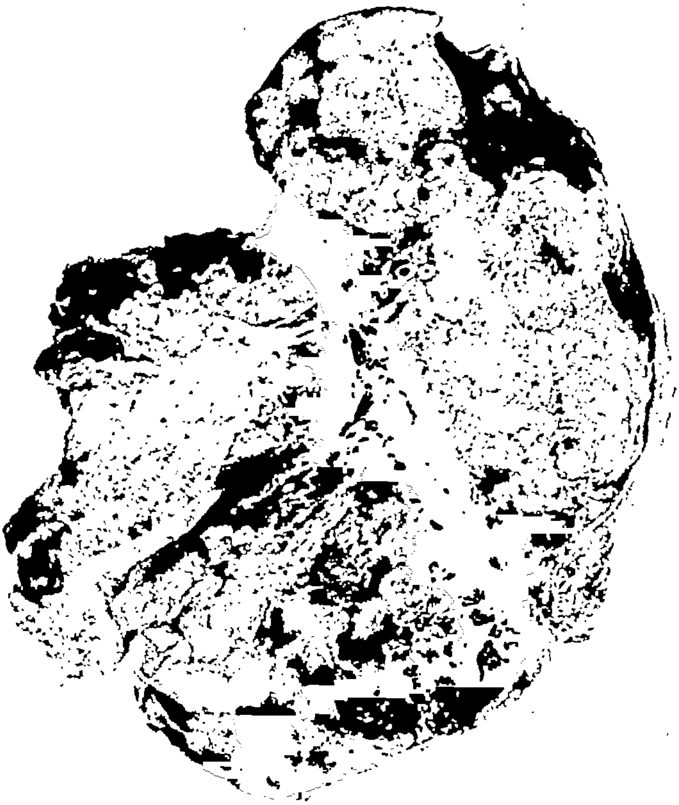

Fig. 3 (Case 4).—Alveolar-cell tumor of both diffuse and nodular type involving the entire right lung. Note the diffuse tumor in the middle lobe and the nodular appearance of the upper and lower lobes.

The remainder of the lobe had scattered nodules averaging 0.5 cm. in diameter. No pleural involvement was found. On microscopic examination the pulmonary alveoli were lined by cells characteristic of alveolar-cell tumor (grade 2). The mucicarmine stain gave negative results. The reticulum stain showed the alveolar septa intact. No fat was seen when the tissue was stained with Sudan IV.

The patient was living and well one year after operation.

Case 4.—A 53-year-old white man came to the clinic with the chief complaint of intermittent dry cough of five years' duration which had turned productive of thick yellow mucus two weeks prior to admission. One year prior to admission during one of his coughing attacks, he had been given penicillin with relief of symptoms. His past history revealed exertional dyspnea of a mild nature for ten years, chronic alcoholism for five years, pneumonia at 14 years of age, and malaria seventeen years prior to the admission. The erythrocytes numbered 4,830,000 and the leucocytes 6,200 per cubic millimeter of blood, 84 per cent of the leucocytes were polymorphonuclear cells, a serologic reaction for syphilis was positive, urinalysis gave negative results, and the roentgenogram showed a dense hemispherical shadow on the right with its flat surface against the posterior axillary portions of the sixth to the tenth ribs. The lateral roentgenologic view revealed emphysema of the middle lobe and contraction of the right lower lobe. Bronchoscopic examination gave negative results. Cytologic examination of three specimens of sputum also gave negative results.

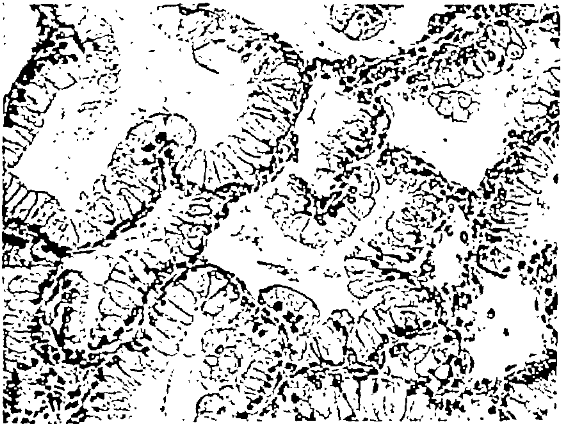

Fig. 4.—Same case as in Fig. 3. Note the marked amount of mucus in the alveolar spaces and the large voluminous cells on intact septa (hematoxylin and eosin, ×200).

Right pneumonectomy was performed. At the time of operation no evidence of metastasis was found. Grossly, the right middle lobe was airless, voluminous, and completely replaced with a pinkish tumor which on cut surface was mucoid. The right upper and lower lobes were not as diffusely involved as was the middle lobe but they contained many nodules that measured 5 mm. to 1 cm. in diameter (Fig. 3). The mucoid appearance was similar to that seen in the middle lobe. Microscopic examination revealed that the pulmonary alveoli in the tumor portions were lined by columnar cells having voluminous cytoplasm and small nucleoli (grade 1 malignancy). The most marked feature was the production of mucus which was evident not only in the tumor cells but also in the adjacent lumina of the uninvolved pulmonary alveoli (Fig. 4). The alveolar septa were not thickened and were easily demonstrated by the reticulum stain. There were many lipophages in the involved as well as in the uninvolved alveoli. All parts of the tumor revealed similar structure.

Six months after operation there was roentgenographic evidence of recurrence in the left lung.

Case 5.—A 30-year-old white woman gave a history of productive cough without hemoptysis for fifteen months. After these symptoms had continued for five months she was sent to a tuberculosis sanatorium because of suggestive roentgenographic evidence obtained by her physician. One month after admission to the sanatorium she began having afternoon fever, night sweats, limited hemoptysis, exertional dyspnea, and pain in the left lower part of the thorax following deep inspiration. After five months in the sanatorium she was dismissed because all investigation for tuberculosis had given negative results. However, she continued having productive cough, afternoon rise of temperature, fatigue, and dyspnea until her admission to the clinic. Prior to admission she had lost nineteen pounds (8.6 kilograms). Physical examination gave essentially negative results on admission except for a few râles in the bases of both lungs. The past history was noncontributory except for a severe bronchitis ten years prior to admission and one attack of pleurisy. The erythrocytes numbered 4,110,000 and the leucocytes 7,300, the value for hemoglobin was 12.4 Gm., a serologic reaction for syphilis was negative, the sedimentation rate was 37, urinalysis gave negative results, and the roentgenogram showed dense infiltration of the left retrocardiac region posteriorly with parenchymal infiltration of the right midpulmonary field. There was also parenchymal infiltration in the upper part of the left lung. On bronchoscopy no lesion could be visualized but biopsy of tissue taken from one of the roentgenographically positive regions proved the lesion to be alveolar-cell tumor. Cytologic studies of sputum and bronchial secretions obtained the same day were all positive for carcinoma cells that were consistent with the diagnosis of alveolar-cell tumor. Acid-fast stains of the sputum were negative for tubercle bacilli.

Because of the nature of the lesion it was decided to do a segmental resection of the involved lobes on both sides. Left lower lobectomy was done first. Two months later, right upper lobectomy with segmental resection of the right lower lobe was performed. On gross examination two-thirds of the left lower lobe was replaced by a pinkish-white, airless mass. The remaining lobe appeared to be normal grossly at the time of operation. The pleura was uninvolved. The right upper lobe was also partially replaced with pinkish tumor which tended to show nodularity, with the nodules ranging from 0.5 to 1 cm. in diameter. There was some puckering of the pleura but otherwise it was uninvolved. Microscopically the tumors in the different lobes presented similar histologic appearances. The cells had pinkish cytoplasm and fairly regular nuclei (grade 2). The tumor was thrown into papillary infoldings. The reticulum stain showed that the septa were intact. A moderate amount of mucus could be demonstrated by the mucicarmine stain.

The patient died on the sixth postoperative day of right-sided heart failure.

CASE 6.—A 34-year-old white woman came to the clinic with the chief complaint of recurrent pain in the back for a period of two months. For four months she had noticed a swelling in the right cervical region. Biopsy of a node at that time disclosed hyperplastic lymphadenitis. Her one respiratory complaint was cough for three years. Her past history was noncontributory except for right-sided pleurisy seventeen years prior to admission. The erythrocytes numbered 4,490,000 and the leucocytes 9,500, the results of urinalysis were negative, the leucocyte differential count was normal, the blood phosphorus measured 3.9 mg. per 100 c.c., the sedimentation rate was 81, and the roentgenograms of the thorax revealed a lesion in the left lung posterior to the hilum with some appearance of pleural involvement. Bronchoscopy gave negative results. Cytologic examinations of the sputum and bronchial secretions were not done.

Left lower lobectomy was done. No evidence of metastasis at the time of operation was noted. On gross examination the entire lower lobe was voluminous, solid and airless. The cut surface was pinkish and had the consistency of liver. There was some nodularity. On the anterior surface there was puckering of the pleura but otherwise the pleura was uninvolved. Histologically the alveolar septa were lined by cells having pinkish cytoplasm which in places was clear. The cells were thrown in papillary infolds. The reticulum stain revealed intact alveolar septa. The stain for fat showed fat in the interalveolar septa but none in the tumor cells. The tumor cells had fairly large nuclei and varied considerably in size (grade 3). The mucicarmine stain gave positive results in some parts of the section.

Four years after lobectomy cervical lymphadenopathy developed. Biopsy revealed Hodgkin's disease. The patient died two years later. Necropsy was not done.

CASE 7.—A 62-year-old white woman gave a history of nonproductive cough of seven months' duration. Her cough was aggravated by walking, but there was no history of dyspnea

OBSTRUCTING INTRABRONCHIAL HODGKIN'S DISEASE

Case Report

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Herein is reported a case of an unusual endobronchial tumor which was shown to be Hodgkin's disease by bronchoscopic biopsy specimen. A left supraclavicular lymph node biopsy supported this diagnosis. To our knowledge the literature has recorded only one other case in which an ante-mortem diagnosis of endobronchial Hodgkin's disease has been made in this manner. Hammond,[1] in 1941, reported a 15-year-old boy with a partial tracheal obstruction and a mediastinal mass. Bronchoscopy was performed twice for the diagnosis and to relieve the obstruction. A right tracheal-wall pedunculated tumor just above the carina and acting in a ball-valve manner on the right main-stem bronchus was found. The second bronchoscopic biopsy revealed Hodgkin's disease. X-ray therapy was instituted.

Autopsied cases of intrabronchial Hodgkin's disease have been described. Murchison,[2] in 1870, reported a 6-year-old girl in whom the smaller bronchial walls were replaced with "adventitial tissue" typical of Hodgkin's tumor. In 1885, Ribbert[3] recorded narrowing of the bronchial tree by intramural Hodgkin's disease. There may be partial[4, 5, 6] or complete[7-10] bronchial occlusion from extra.[11, 12, 13] or intramural, tumor causing partial or total pulmonary atelectasis.[10, 12, 14] Tracheal involvement[1, 3, 15] and tracheoesophageal fistula[16] have been reported.

The incidence of Hodgkin's disease is given as 0.24 per cent by Wallhauser[17] (15,783 routine autopsies) and as 0.33 per cent by Jackson[18] (18,668 routine autopsies). *Intrathoracic involvement* (autopsy and chest roentgenogram) varies from 40 per cent to 80 per cent.[4, 10, 14, 19, 20] In 212 cases, Goldman[21] found 30 of 89 (33 per cent) "early cases" and 94 of 124 (76 per cent) "late cases" had intrathoracic Hodgkin's disease. Intrabronchial involvement was found in 2 of 18 autopsies by Moolten[10]; 2 of 16 autopsies by Krueger and Meyer[14]; and 2 of 10 autopsies by Fraenkel and Much[22] in cases of known Hodgkin's disease (over-all average of 13.6 per cent). Moolten believed that bronchial involvement must be thought of as among the most typical features of pulmonary Hodgkin's disease.

Pathologically Hodgkin's disease is now generally classified in the lymphoma group.[23, 24] The pulmonary lesions may be primary (autochthonous), originating from the lymph nodules within the lung parenchyma or submucosa of the bronchi or secondary, by direct extension or metastatic spread of the tumor cells.[19, 23]

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Pulmonary Hodgkin's disease has been macroscopically classified in essentially similar manners by various authors.[4, 16, 18, 20] Hartfall's[26] classification is listed:

1. Root infiltration from a mediastinal glandular mass.
2. Massive intrapulmonary Hodgkin's disease.
3. Diffuse fibrous infiltration (which proves to be Hodgkin's disease microscopically).
4. Discrete or nodular disseminated Hodgkin's disease.

The lesion then progresses:

1. By direct extension into the lung.
2. By extension along the bronchi.
3. Lymphatic spread via:
   a. peribronchial
   b. perivascular
   c. subpleural
   d. interstitial
4. By vascular involvement, for example, by entry into the bronchial or pulmonary veins or arteries.
5. By a combination of the preceding.

Others have divided the disease according to the microscopic appearance and have made prognostic correlations.[13, 18]

Willis[25] lists the microscopic spread of malignant tumors in general in the following ways: (1) Direct extension into and infiltration of the tissue spaces along anatomic cleavage planes by the tumor cells with progression in size of the lesion. This is always the initial and most fundamental mode of spread. (2) Invasion of, and progression along, the lymphatic vessels. (3) Invasion of the veins and capillaries with thrombosis and tumor emboli. Willis believed that Hodgkin's disease may spread in the same manner. ''Hilar lesions may surround and invade the main bronchi, and so may be indistinguishable grossly from bronchogenic carcinoma.'' The term ''pan-bronchitis'' has been used for the total replacement of the bronchial wall with tumor cells and the inflamed appearance of the mucosa.[27, 28]

The following case correlates the clinical features of an obstructing bronchial tumor with the diagnosis of Hodgkin's disease. Such correlation has been reported previously only in autopsied cases, except for the one reported by Hammond.

CASE REPORT

R. G. H., a 24-year-old white man, entered the Veterans Hospital, Portland, Ore., on July 18, 1949, for treatment of a bronchiogenic carcinoma.

On May 7, 1949, the patient was hospitalized elsewhere with a right lobar pneumonia (chills, temperature, 105° F.). One month prior to admission, he had had cough, fatigue, and irritability. After six days of hospitalization and Crysticillin therapy, he returned home feeling well. On May 23, 1949, the patient was readmitted because of sudden right pleuritic pain and constant low-grade fever. A chest roentgenogram revealed clouding in the right lower lung field. Despite Crysticillin and aureomycin therapy, the patient maintained a low-grade fever with elevations to 102° to 103° F. Two thoracenteses were performed, the first yielding no fluid, and the second, 12 c.c. of sterile sanguineous purulent fluid. Repeated chest roentgenograms revealed no change.

right hilar mass), and 1,500 r over the left cervical port (lymph node biopsy area) using a Thoraeus filter. The patient's blood picture was followed by a complete blood cell count every two to four days while under treatment. The white blood cell count varied from 5,000 *to 9,000 with an essentially normal differential white blood cell count, the eosinophil count* never exceeding 4 per cent. The hemoglobin rose from 12.5 to 14.5 gram per cent.

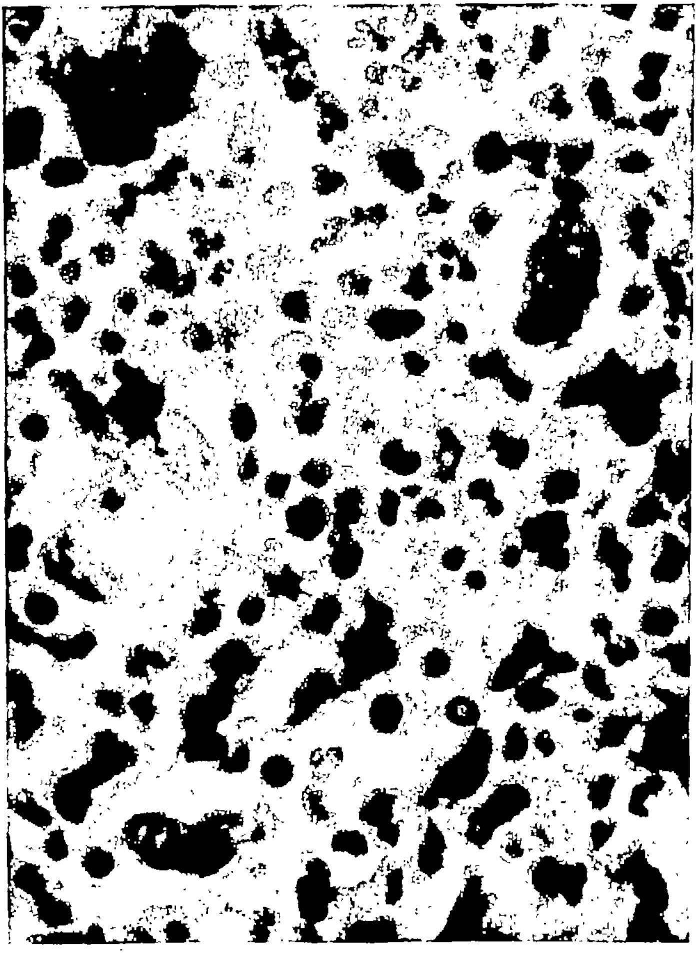

Fig. 2.—Photomicrograph of bronchial biopsy specimen revealing characteristic cellular elements of Hodgkin's disease. ×800.

The patient received no other treatment except general supportive therapy and one course of crystallin penicillin of 100,000 units every three hours from July 20 to Aug. 3, 1949. The temperature graph revealed an average periodic evening rise to 99.8° F. during this same period, remaining normal thereafter.

Clinically the patient had gained weight, had become cheerful and optimistic. There was complete pulmonary expansion with good breath sounds over the right chest. Patient was therefore discharged.

On Jan. 9, 1950, approximately four months after completion of the x-ray therapy, the patient returned for re-examination by the Tumor Board. He had no complaints, had maintained his weight, and was working. Clinical examination was within normal limits. A chest roentgenogram was essentially the same as on Aug. 31, 1949. Bronchoscopy at this time revealed normal bronchial trees bilaterally; all orifices were identified on the right and there did not appear to be any mucosal irregularity. The patient was discharged for further Tumor Board follow-up study.

DISCUSSION

Several points are of interest in the preceding case.

1. As with any type of obstructing bronchial lesion, the initial phase was of a partial collapse, stasis of bronchial secretions, and finally pneumonitis, this last causing symptoms that forced the patient to seek medical aid. The pneumonitis cleared on antibiotic therapy only to reappear because the basic lesion remained unchanged. Finally, as the obstruction became complete, antibiotic therapy had no appreciable effect.

2. In the other case reported in the literature analogous to the preceding one, despite a seemingly adequate biopsy (as also in our case) on the first bronchoscopy, a microscopic diagnosis could be made only of inflammation. A second bronchoscopy and biopsy were needed for the true diagnosis.

3. This case exemplifies the paucity of physical signs pathognomonic of classical Hodgkin's disease. Also the dramatic response of this disease to adequate x-ray therapy.

4. Routine bronchoscopy in all cases of Hodgkin's disease, even without clinical evidence of bronchial obstruction, might prove of value diagnostically, therapeutically, and statistically.

5. The fact that primary pulmonary Hodgkin's disease, though certainly not common, can simulate acute inflammatory disease, pulmonary abscess, primary tuberculosis, and bronchiogenic and metastatic carcinoma[18] cautions the diagnostician to use all facilities in making an accurate etiological diagnosis of any pulmonary lesion.

SUMMARY

A case of obstructing intrabronchial Hodgkin's disease diagnose
choscopic biopsy specimen is reported. A review of the literature

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A TECHNIQUE FOR THE SURGICAL TREATMENT OF CONGENITAL EVENTRATION OF THE DIAPHRAGM IN INFANCY

REPORT OF A CASE

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THE surgical management of congenital eventration of the diaphragm in infancy has rarely been the subject of published reports. Only two cases that have undergone successful operation were discovered in the literature, both of these appeared in the past two years.

This case is reported because it differs from the previous two in that it occurred on the left side, the infant was younger, and there was a different type of operative technique employed.

Bisgard[1] described the first surgical correction of this condition in an infant aged 6 weeks. His method consisted of a transthoracic operation for a right-sided eventration with plication of the diaphragm using three superimposed rows of interrupted mattress sutures of silk. The pleat, thus formed, was turned downward between the diaphragm and the liver. The diaphragm was of normal appearance consisting of muscle and an excellent result was reported twenty-two months following the operation.

State[2] has recently described a transabdominal technique by means of which he corrected a right-sided eventration in a male infant 6 weeks of age. Exposure was made through a subcostal incision. The diaphragm was found to be of normal muscular development but high in position reaching to the second interspace anteriorly. The anterior portion of the diaphragm was brought down and sutured to the anterior costal margin. The posterior part of the diaphragm was then united to the right crus and renal fascia. To prevent pressure on the newly formed diaphragm, only the skin of the abdominal wall was closed. The incisional hernia, thus created, was repaired a year later.

CASE REPORT

M. S., *a 9-day-old white female infant was referred** to the Children's Hospital on May 17, 1949. Delivery had been difficult and prolonged. The child was cyanotic at birth. Voluntary respirations were established finally, after a trial of several hours with artificial measures. Following this the baby again became cyanotic whenever food was offered or upon crying. Oxygen was administered most of the time. There was a progressive weight loss from 7 pounds 4 ounces at birth, to 6 pounds, 2 ounces.

Admission examination showed a fairly well-developed baby who breathed with obvious difficulty. No difference was noted between the expansion of the two sides of the thorax. The percussion note was hyperresonant on the left although good breath sounds could be heard on that side. The heart tones were best heard at the right border of the sternum.

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The ventilation during exertion was apparently sufficient to prevent excessive accumulation of carbon dioxide. The rise in CO_2 tension which was seen in a few instances cannot be considered as abnormal. The accumulation of lactic acid during exercise, as shown by the fall in whole blood buffer base, was not excessive for individuals who are on the whole poorly trained.

The rise in saturation in three instances (including the case with a low resting value) must be due to improvement in alveolar ventilation/perfusion relationships under the stimulus of exercise. Such a rise is not uncommonly seen in moderate degrees of emphysema. Factors leading to such improvement are increase in alveolar ventilation, more intimate alveolar mixing, and increased pulmonary capillary surface across which diffusion must take place. It can be concluded that in each of the patients studied ventilatory abnormalities were present, which in all but two instances lead to deficient blood oxygenation in the lungs, either at rest or during moderate exercise, or both. In spite of this all but two patients were able to lead useful lives and some of them performed moderately severe physical exercise.

We are grateful to Dr. William B. Seaman of the Mallinckrodt Institute of Radiology for his help in the interpretation of the radiograms.

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